986 nnual eport

Division of Computer Research and Technology

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
National Institutes of Health

National Institutes of Health (U.S.) Annual report

Division of Computer Research and Technology

Projects FY86

Z01CT00001-15	LSM	Automated Data Processing of Medical Language
Z01CT00002-16	LAS	Computer-Aided Analysis of Electrocardiography
Z01CT00003-15	LAS	Computer Systems for Nuclear Medicine
Z01CT00004-15	LAS	Analysis of Physiological Signals
Z01CT00005-16	LAS	Mathematical Models of Binding Equilibria
Z01CT00008-12	LSM	Cluster Analysis
Z01CT00010-10	LAS	Mathematical and Computational Methods: Solving Nonlinear Equations
Z01CT00011-12	LSM	Discrete Mathematics and Applications
Z01CT00013-12	LSM	Multivariate Statistical Analysis
Z01CT00014-19	PSL	Instrumental Analysis
Z01CT00017-14	PSL	Biophysical Analysis
Z01CT00021-15	PSL	Correlation Function Spectroscopy/Laser Light Scattering
Z01CT00022-19	PSL	Consulting Services
Z01CT00024-11	PSL	Studies in Mathematics and Statistics
Z01CT00026-11	PSL	Molecular Forces in Cellular Assembly
Z01CT00039-09	LSM	Linear Methods in Statistics
Z01CT00042-08	LAS	Image Processing in Electron/X-Ray/EEL Spectroscopy Microscopy
Z01CT00044-08	LAS	Mathematical Modeling of Substrate Transport
Z01CT00045-08	LAS	The Solution of Reaction-Diffusion Systems in Biology
Z01CT00050-07	CSL	Computer Support for Flow Cytometry/Electronic Cell Sorter (FC/ECS)
Z01CT00051-07	CSL	Cardiac Scintillation Probe

Z01CT00054-07	CSL	Medical Intensive Care Unit Patient Monitoring Computer System
Z01CT00056-07	CSL	Distributed Laboratory Data Acquisition and Control System
Z01CT00065-07	CSL	Medical Information Technology Project
Z01CT00066-07	PSL	Computerized Typesetting of Scientific Papers
Z01CT00078-05	OD	Electronic Typesetting Methods
Z01CT00080-06	CSL	Computer Analysis of Gel Electrophoresis
Z01CT00081-06	CSL	Rehabilitation Medicine Department Computer System
Z01CT00082-06	CSL	Image Processing of Electron Micrographs
Z01CT00090-05	CSL	Molecular Graphics, Computer Modeling, and Sequence Analysis
Z01CT00092-05	CSL	Virus Structure as Determined by Image Processing of Electron Micrographs
Z01CT00098-05	LAS	Computer-Based Monitoring of the CNS in Critically Ill Patients
Z01CT00099-05	CSL	Automated Management of Critically Ill Patients
Z01CT00105-04	CSL	Medical Image Data Compression
Z01CT00108-04	PSL	Studies on the Effect of Solvent Around Biological Macromolecules
Z01CT00111-04	LSM	Nonparametric Statistics
Z01CT00119-03	PSL	Membrane Fusion
Z01CT00120-03	LSM	Computer Graphics and Mathematical Applications
Z01CT00121-03	LAS	Applications of Personal Computers to Laboratory Research
Z01CT00122-03	OD	Computerized Typesetting Consultation
Z01CT00123-03	CSL	Cardiac Ultrasound Image Processing
Z01CT00124-03	CSL	Personal Computer System for Automatic Coronary Venous Flow Measurements

Z01CT00128-02	CSL	Urinalysis Data Gathering System
Z01CT00129-02	PSL	Membrane Transport
Z01CT00130-02	PSL	Development of Apollo Computer System for Modeling Macromolecules
Z01CT00131-02	LSM	DNA Sequence Analysis and Related Methods
Z01CT00132-02	LSM	Algorithms and Other Methods for Biomathematical Computing
Z01CT00133-02	OD	Personal Computer Implementation on Local Area Networks
Z01CT00137-02	CSL	Cataract Quantitation Using Image Processing
Z01CT00138-02	CSL	Brain Image Registration
Z01CT00139-02	CSL	Advanced Laboratory Workstation
Z01CT00140-02	CSL	NIH Campus Area Network
Z01CT00141-02	CSL	Expert Systems in Medicine
Z01CT00142-02	CSL	Retina Metabolism Research System
Z01CT00143-01	LSM	Consulting Services
Z01CT00144-01	OD	Personal Computer Bibliographic Systems
Z02CT00145-01	OD	Bibliographic Retrieval Systems on Local Area Networks
Z02CT00146-01	OD	Understanding Protein Architecture through Simulated Unfolding
Z01CT00147-01	PSL	Cell Membrane Studies
Z01CT00148-01	CSL	Neuromagnetometer Computer System
Z01CT00149-01	CSL	Expert System Techniques
Z01CT00150-01	CSL	Nuclear Medicine Computer System
Z01CT00151-01	CSL	Audiology ABR Analysis and Interpretation Expert System

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CT00001-15 LSM

PERIOD COVERED

October 1, 1985 through September 30, 1986.

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Automated Data Processing of Medical Language

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)

M. G. Pacak Supv. Computer Systems Analyst LSM DCRT

COOPERATING UNITS *(if any)*

A. W. Pratt	Director	OD	DCRT	E. Jaffe	Chief, Hema. Sec.	DCBD	NCI
G. Dunham	Comp. Prog.	LSM	DCRT	D. Henson	Program Director	DCPC	NCI
S. Harper	Comp. Prog.	LSM	DCRT				

LAB/BRANCH

Laboratory of Statistical and Mathematical Methodology

SECTION

Medical Information Science Section

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, Maryland 20892

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
1.5	1.5	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The major objective of the project is the development of methods for the automatic processing of natural medical language. This involves both development of algorithms for parsing and representing natural text, and creation of computer dictionaries and other data bases for medical specialties such as surgical pathology.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CT00002-16 LAS

PERIOD COVERED

October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Computer-Aided Analysis of Electrocardiography

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

J.J. Bailey	Chief, MAS	LAS	DCRT
M.R. Horton	Computer Systems Analyst	LAS	DCRT

COOPERATING UNITS *(if any)*

Framingham Heart Study; Georgetown Medical Center; Glasgow Royal Infirmary

LAB/BRANCH

Laboratory of Applied Studies

SECTION

Medical Applications Section

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.35	1.00	0.35

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

These studies are directed toward accessing the predictive accuracy of ECG criteria and the clinical utility of ECG computer programs. Further investigations involve the design of new criteria using well documented populations and statistical techniques.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CT00003-15 LAS

PERIOD COVERED

October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Computer Systems for Nuclear Medicine

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

M.A. Douglas	Computer System Analyst	LAS DCRT
J.J. Bailey	Chief, MAS	LAS DCRT

COOPERATING UNITS *(if any)*

Nuclear Medicine, Clinical Center; NHLBI/CB

LAB/BRANCH

Laboratory of Applied Studies

SECTION

Medical Applications Section

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.15	1.00	0.15

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project involves computer-based mathematical analysis, pattern recognition, and image processing in support of diagnostic activities in the Nuclear Medicine Department of the Clinical Center and collaborating Institutes. Diverse applications include: computerized ECG-gated radionuclide ventriculography, myocardial perfusion scintigraphy, tagged monoclonal antibody studies, brain anatomy studies and pulmonary ventilation-perfusion relationships. Technical developments include: evaluation of the use of personal computers in nuclear medicine imaging; the specification and development of a new general purpose image processing facility for the Nuclear Medicine Department; and the development of methods to facilitate automated multimodality image registration of the head and other anatomy.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CT00004-15 LAS

PERIOD COVERED

October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Analysis of Physiological Signals

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

E.W. Pottala	Electrical Engineer	LAS	DCRT
J.J. Bailey	Chief, MAS	LAS	DCRT
J.A. Dvorak		LPD	NIAID

COOPERATING UNITS *(if any)*

Laboratory of Parasitic Disease, NIAID
Division of Cardio-Renal Drug Products, FDA

LAB/BRANCH

Laboratory of Applied Studies

SECTION

Medical Applications Section

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.35	1.00	0.35

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project involves the development and application of minicomputer-based signal processing techniques for analysis of physiological signals, (e.g., electrocardiogram, electromyogram, and electroencephalogram).

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CT00005-16 LAS

PERIOD COVERED

October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 charactars or less Title must fit on one line betwaen the borders.)*

Mathematical Models of Binding Equilibria

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

J.E. Fletcher Chief, Applied Math. Sec LAS DCRT

COOPERATING UNITS *(if any)*

LAB/BRANCH

Laboratory of Applied Studies

SECTION

Applied Mathematics Section

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.11	0.05	0.06

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unraducad type. Do not exceed the space provided.)*

The objective of this project is the study of mathematical models of ligand-receptor or ligand-macromolecule binding studies at equilibrium. Appropriateness of various model fitting criteria are studied and general guidelines and computational algorithms are designed for computer-aided interactive model fitting.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CT00008-12 LSM

PERIOD COVERED

October 1, 1985 through September 30, 1986.

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Cluster Analysis

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*

(Name, title, laboratory, and institute affiliation)

M. B. Shapiro Research Mathematician LSM DCRT

COOPERATING UNITS *(if any)*

LAB/BRANCH

Laboratory of Statistical and Mathematical Methodology

SECTION

Statistical Methodology Section

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, Maryland 20892

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
0.7	0.7	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The main objective of this project is the application of computer cluster analysis and related methods to NIH research problems.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CT00010-10 LAS

PERIOD COVERED

October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Mathematical and Computational Methods: Solving Nonlinear Equations

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

R.I. Shrager	Research Mathematician	LAS DCRT
Behrooz Kamgar-Parsi	Guest Worker	LAS DCRT

COOPERATING UNITS *(if any)*

NHLBI/LB; NIADDK/LCP; U. Of MD Computer Science Dept.

LAB/BRANCH

Laboratory of Applied Studies

SECTION

Applied Mathematics

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.15	1.00	0.15

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Methods are developed for solving nonlinear equations frequently encountered at NIH. These equations are usually encountered in the context of constrained nonlinear least squares problems or in the numerical solution of nonlinear differential equations. Related problems, such as asymptotic error analysis and the efficient treatment of sparse matrix systems, are also considered.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CT00011-12 LSM

PERIOD COVERED

October 1, 1985 through September 30, 1986.

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Discrete Mathematics and Applications

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)

G. Hutchinson Supv. Res. Mathematician LSM DCRT

COOPERATING UNITS *(if any)*

LAB/BRANCH

Laboratory of Statistical and Mathematical Methodology

SECTION

Biomathematics and Computer Science Section

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, Maryland 20892

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
0.4	0.4	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The project objective is to develop mathematical theory and computational techniques using discrete mathematics (algebra, combinatorics and graph theory), and to apply such methods to appropriate problems of biomedical research and computer science.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

01 CT00013-12 LSM

PERIOD COVERED

October 1, 1985 through September 30, 1986.

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Multivariate Statistical Analysis

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*

(Name, title, laboratory, and institute affiliation)

J. E. Mosimann Chief, LSM LSM DCRT

COOPERATING UNITS *(if any)*

G. Campbell Senior Staff Fellow LSM DCRT

LAB/BRANCH

Laboratory of Statistical and Mathematical Methodology

SECTION

Office of the Chief

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, Maryland 20892

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
0.6	0.6	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The objective of this project is the study of multivariate ratios or proportions.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 CT00014-19 PSL

PERIOD COVERED

October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Instrumental Analysis

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator) (Name, title, laboratory, and institute affiliation)*

George H. Weiss, Ph.D., Chief, PSL, DCRT
V. Bloomfield, Ph.D., Univ. of Minnesota; A. Byrd, Ph.D., NIDR; M. Dishon, Ph.D., Weizmann Institute; J. A. Ferretti, Ph.D., NHLBI; J. E. Kiefer, PSL, DCRT; U. Shmueli, Ph.D., Tel-Aviv Univ., Israel

COOPERATING UNITS *(if any)*

LAB/BRANCH

Physical Sciences Laboratory

SECTION

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.5	0.4	0.1

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project includes a number of different investigations. We have initiated a project together with Dr. Ferretti (NHLBI) on the choice of optimal apodization functions for the measurement of areas and volumes in Fourier transform NMR. Apodization functions are used to preprocess data before analyzing their physical content. We have found that Gaussian apodization functions leads to a considerable increase in the precision of area measurements under curves generated in one-dimensional NMR. This agrees with earlier observations for which no theory has been available. Together with Dr. Ferretti we have completed an invited review article on optimal methods for the measurement of spin-lattice relaxation times in NMR.

In a joint project with Professor Shmueli of Tel-Aviv University we have further developed the theory of exact representations of probability densities that are used in crystallography. We have calculated a number of such densities useful in the application of intensity statistics, and are presently working on representations of the densities of phase invariants used in direct methods of phase determination. Progress on this problem is slow because of the complicated calculations that are required.

We have, together with Professor Bloomfield, a visiting FIC Fellow, initiated a study of the effects of pore size distribution relative to the size of macromolecules in gel electrophoresis. This study is aimed at the determination of qualitative effects in gel electrophoresis, and involves a combination of simulation and exact methods of solution.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 CT00017-14 PSL

PERIOD COVERED
October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Biophysical Analysis

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*
Ralph J. Nossal, Ph.D., Research Physicist, PSL, DCRT
J. Hofrichter, Ph.D., NIADDK/LCP; G. H. Weiss, PSL, DCRT; B. Trus, LAS, DCRT;
S. Havlin, Ph.D., Bar-Ilan Univ., Israel; S. H. Chen, Dept Nucl. Engr., MIT;
C. Glinka, Reactor Div., NBS; A. Bunde, and H. E. Stanley, Physics Dept., Boston University

COOPERATING UNITS *(if any)*

LAB/BRANCH
Physical Sciences Laboratory

SECTION

INSTITUTE AND LOCATION
DCRT, NIH, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.8	0.7	0.1

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

We have further developed a scheme utilizing small angle neutron scattering (SANS) to probe interactions between macromolecules in highly concentrated protein solutions. Using this technique we have systematically studied properties of bovine serum albumin (BSA) samples to test the theoretical analysis thus is used to extract molecular size and charge from experimental data. Studies also were performed on hemoglobin (Hb) solutions, the results of which were employed to devise techniques for examining protein interactions within intact erythrocytes and other biological vesicles. The contrast match point for vesicle membranes has been determined and detection of protein aggregates in deoxygenated sickle red blood cells was demonstrated. Several investigations based on this methodology now are in progress.

We have undertaken investigations into the properties of polymer networks and related amorphous structures. For this purpose we have developed mathematical models to describe the formation of cytoskeletal networks. These allowed us to investigate complex relationships between nucleation. Polymerization, crosslinking, chain termination and chain scission procedures were developed for obtaining "elasticity contours" (e.g., dependences of shear modulus on Ca++ concentration), which are needed for theories of cell movement. Quantitative gelation assays for assessing the activity or cytoskeletal binding proteins also were analyzed.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CT00021-15 PSL

PERIOD COVERED

October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 charecters or less. Title must fit on one line between the borders.)*

Correlation Function Spectroscopy/Laser Light Scattering

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

Ralph J. Nossal, Ph.D., Research Physicist, PSL, DCRT
R. Bonner, Ph.D., BEIB, DRS; G. Ehrenstein, Ph.D., LB, NINCDS; N. Gershfeld, LBP, NIADDK; S. Havlin, Ph.D., Bar-Ilan Univ., Israel; J. Russell, Ph.D., LNN, NICHHD; G. W. Weiss, Ph.D., DCRT/PSL

COOPERATING UNITS *(if any)*

LAB/BRANCH

Physical Sciences Laboratory

SECTION

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.4	0.3	0.1

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

In many in vivo clinical and research uses of light, incident radiation is applied to the interface between a turbid tissue and a transparent medium. Light that diffuses back to this interface and into the external transparent medium provides a noninvasive means to examine the parameters of photon diffusion within the tissue. Laser Doppler blood flow monitors, in particular, work on this principle. We have developed an analytical theory that enables calibration of such instruments from measurements of reflected light on the tissue surface. The theory relates such quantities as surface emission profile, sampling depth, and expected path length of migrating photons, to the scattering and absorption parameters of a tissue. The theoretically predicted wavelength dependence of those quantities has been verified experimentally.

Also, dynamic light scattering studies have been performed in collaboration with Dr. N. Gershfeld (NIADDK/LBP). The major emphasis of this investigation has been on the structural transitions that occur in lipid-water suspensions. The movement of polystyrene beads has been used to probe the structure of the suspensions. Transformations have been seen in bulk dimyristoylphosphatidyl-glycerol (DMPG) water systems at the same temperatures where discontinuities in surface pressure are discerned in film balance studies. Below the transition temperatures the dispersed lipid seems to form a jelly-like slurry, whereas above those temperatures the suspensions contain lipid vesicles. Dr. Gershfeld has performed surface film studies that indicate similar transformations may occur in the growth of biological cells.

Other dynamic light scattering studies have been initiated. A particularly promising collaboration (with G. Ehrenstein and J. Russell) concerns the release of peptides from neurosecretory vesicles.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CT00022-19 PSL

PERIOD COVERED

October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Consulting Services

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

George H. Weiss, Ph.D., PSL, DCRT
J. E. Kiefer, PSL, DCRT; R. A. Brooks, Ph.D.,NINCDS

COOPERATING UNITS *(if any)*

LAB/BRANCH

Physical Sciences Laboratory

SECTION

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.2	0.0	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

We have developed a theory that allows one to estimate measures of precision for rate constants found from PET scan measurements. The theory also allows one to design optimal experiments for such estimates.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CT00024-11 PSL

PERIOD COVERED

October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 chererters or less. Title must fit on one line between the borders.)*

Studies in Mathematics and Statistics

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigetor.) (Name, title, laboretory, and institute affiliation)*

George H. Weiss, Ph.D., PSL, DCRT
E. A. diMarzio, Ph.D., National Bureau of Standards; R. J. Gaylord, Ph.D., Univ. of Illinois; S. Havlin, Ph.D., Bar-Ilan Univ., Israel; J. E. Kiefer, PSL, DCRT; A. Szabo, Ph.D., NIADDK

COOPERATING UNITS *(if any)*

LAB/BRANCH

Physical Sciences Laboratory

SECTION

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.5	0.4	0.1

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type Do not exceed the space provided)*

We have continued work on projects related to the theory of reaction rates for chemical reactions. Present projects include the study of statistical properties of the displacement of diffusing particles in a field of static traps, and the theory of survival times of particles in a field of static traps subjected to time-varying forces. A second project relates to the microscopic kinetics of entangled polymers. Together with Dr. Szabo we are writing a review of first passage time problems in chemical physics.

DEPARTMENT OF HEALTH AND HUMAN SERVICES · PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 CT00026-11 PSL

PERIOD COVERED
October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Molecular Forces in Cellular Assembly

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*
V. Adrian Parsegian, Ph.D., PSL, DCRT
E. Barouch, Ph.D., Clarkson Univ., NY; E. A. Evans, Ph.D., U. British Columbia, Canada; S. Gruner, Ph.D., Princeton Univ., NJ; A. L. Harris, Ph.D., PSL, DCRT and J. Hopkins Univ., MD; R. P. Rand, Ph.D., Brock Univ., Canada; D. Rau, Ph.D., NIADDK; J. Zimmerberg, Ph.D., PSL, DCRT

COOPERATING UNITS *(if any)*

LAB/BRANCH
Physical Sciences Laboratory

SECTION

INSTITUTE AND LOCATION
DCRT, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.2	1.2	0.0

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

One usually thinks of cell membrane lipids in the form of the lamellar sheets in which they are orginally found. It appears from our recent work that the addition of relatively small amounts of non-polar hydrocarbons can create non-lamellar arrangements similar to those that occur during such membrane fusion processes as cellular secretion. We have determined the chemical potential of phospholipids in the inverted hexagonal structure finding that the lipid hydrocarbon chains pack to fill space with negligible strain. Measuring the work of bending lipid layers we have found that their bending elasticity modulus is essentially the same for planar structures as for layers with small spontaneous radii of curvature.

In these lipid systems we find that the work of bringing bodies together is the hydration force of removing structured water solvent from their surfaces. We have been able to modify forces between DNA macromolecules by altering the entropy of water in the bathing solution. To do this we have used different anionic solutes--"chaotropic" perchlorate, chloride, and order-forming sulphate --to change the entropy of the bathing medium. We have found that relatively small changes in the ionic composition of the bathing solution change the properties of water solvent enough to control molecular assembly. These experimental findings are tightly coupled to theoretical analyses to formulate and to compute interactions. We have evaluated the accuracy of the well-known Derjagin approximation for converting the interaction between curved surfaces into that between planar surfaces of the same material.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

Z01 CT00039-09 LSM

PERIOD COVERED

October 1, 1985 through September 30, 1986.

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Linear Methods in Statistics

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*

(Name, title, laboratory, and institute affiliation)

J. D. Malley Mathematical Statistician LSM DCRT

COOPERATING UNITS *(if any)*

LAB/BRANCH

Laboratory of Statistical and Mathematical Methodology

SECTION

Statistical Methodology Section

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, Maryland 20892

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
0.6	0.6	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The objective of this project is to study new algebraic methods in statistics and their applications to biomedical research.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

Z01 CE00042-08 LAS

PERIOD COVERED

October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less Title must fit on one line between the borders.)*

Image Processing in Electron/X-Ray/EEL Spectroscopy Microscopy

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

M.A. Douglas	Computer Systems Analyst	LAS	DCRT
S.P. Chock	Expert Consultant	LNC	NCDS

COOPERATING UNITS *(if any)*

LAB/BRANCH

Laboratory of Applied Studies

SECTION

Medical Applications Section

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.60	0.50	0.10

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project is directed toward the development of computer-based mathematical and statistical analyses, pattern recognition, and image processing of data, principally x-ray micrography and electron energy loss spectra, or from the electron/light microscopy images of biological specimens.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 CT00044-08 LAS

PERIOD COVERED
October 1, 1985 to September 30,1986

TITLE OF PROJECT *(80 characters or less Title must fit on one line between the borders.)*
Mathematical Modeling of Substrate Transport

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

J.E. Fletcher	Chief, Applied Math. Sec.	LAS	DCRT
R.W. Schubert	Prof. Biomed. Engineering	LTU	Biomed/Eng

COOPERATING UNITS *(if any)*
Dept. of Biomedical Engineering, LTU
Laboratory of Biochemistry, NHLBI

LAB/BRANCH
Laboratory of Applied Studies

SECTION
Applied Mathematics Section

INSTITUTE AND LOCATION
DCRT, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.20	0.85	0.35

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Mathematical models of microcirculatory structure and function are developed from conceptual models into computer simulation models. The simulation model results are interpreted in terms of microcirculatory physiology. Project objectives are to study whole organ response and organ tissue level phenomena by means of mathematical models in an effort to determine relationships between variables that govern the organ response to physiologic challenges.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 CT00045-08 LAS

PERIOD COVERED

October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

The Solution of Reaction-Diffusion Systems in Biology

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

J.E. Fletcher Chief, Applied Math. Sec. LAS DCRT

COOPERATING UNITS *(if any)*

LAB/BRANCH

Laboratory of Applied Studies

SECTION

Applied Mathematics Section

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.01	0.01	0.00

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project consists of the development of numerical methods and mathematical software for the solution of partial differential equations describing dynamic physiological processes. Adaptive finite element techniques have been generalized and used for models of nerve conduction, oxygen transport in tissue, uptake of macromolecules into the lymphatic system, and in preliminary studies of subsurface contaminant flow. FORTRAN-coded packages implementing these and other techniques are available for use on the major DCRT computers.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CT00050-07 CSL

PERIOD COVERED

October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Computer Support for Flow Cytometry/Electronic Cell Sorters (FC/ECS)

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	L.K. Barden	Electronics Engineer	CSL, DCRT
	W. Gandler	Electronics Engineer	CSL, DCRT
	S. Sharrow	Chemist	IB, NCI
	D. Stephany	Biologist	IB, NCI

COOPERATING UNITS *(if any)*

LAB/BRANCH

Computer Systems Laboratory

SECTION

Processor Design Section

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS	PROFESSIONAL	OTHER
2.0	2.0	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The FC/ECS project involves designing and implementing computer-based data acquisition, management, and analysis systems for Flow Cytometry applications. Our recent effort has been primarily directed toward high volume sites, which are not adequately supported by commercially available data systems. The Immunology Branch, NCI, is the primary site where prototype hardware and software are installed and tested.

During this fiscal year, the two-parameter expansion of the APR data analysis package (developed by CSL for the DLDACS project) has been integrated into our data management and analysis system. Users of this system now have a coherent, flexible means of applying sophisticated data analysis procedures to histogrammed single and dual parameter data.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CT00051-07 CSL

PERIOD COVERED

October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Cardiac Scintillation Probe

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	H. Ostrow	Electronics Engineer	DCRT, CSL
	S. Bacharach	Physicist	CC, NM
	M. Green	Physicist	CC, NM
	R. Bonow	Cardiologist	NHLBI, CB
	R. Canon	Cardiologist	NHLBI, CB

COOPERATING UNITS *(if any)*

LAB/BRANCH

Computer Systems Laboratory

SECTION

Processor Design Section

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS	PROFESSIONAL	OTHER
.1	.1	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The cardiac scintillation probe is a transportable device used to noninvasively monitor left ventricular function. The system uses nuclear medicine ECG-gated scintigraphic techniques and consists of a small detector and microcomputer system mounted on a cart.

The cardiac scintillation probe, when used in conjunction with left ventricular (LV) catheterization, permits simultaneous quantification of the variation of LV volume and pressure allowing parameters such as LV compliance to be continuously monitored. In addition, measurements such as ejection fraction, filling and ejection rates, and temporal relationships can be made.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CT00054-07 CSL

PERIOD COVERED

October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Medical Intensive Care Unit Patient Monitoring Computer System

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	K.M. Kempner	Electronics Engineer	CSL, DCRT
	J.E. Parrillo	Chief, Crit. Care Med. Dept.	CCM, CC
	S.L. Huntley	Supv. Critical Care Tech.	CCM, CC
	J.F. Fessler	Engineering Technician	BEIB, DRS

COOPERATING UNITS *(if any)*

LAB/BRANCH

Computer Systems Laboratory

SECTION

Systems Design Section

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.2	0.2	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The Medical Intensive Care Unit (MICU), administered by the Critical Care Medicine Department in the NIH Clinical Center, receives critically ill patients from clinical programs of NIH. The research goals of this project include the development of techniques for automated patient monitoring and noninvasive measurements of the cardiovascular and respiratory systems. Catheterization studies are performed as necessary to obtain data that are available only through invasive methodology.

The automation of the MICU has aided the medical staff by managing the large amount of data needed for the care of the critically ill patient, performing desired calculations, and allowing measurements that would not otherwise be possible. The multiple-computer system is utilized in support of research protocols, in addition to direct patient care.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 CT00056-07 CSL

PERIOD COVERED
October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Distributed Laboratory Data Acquisition and Control System

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	J.I. Powell	Electronics Engineer	CSL, DCRT
	W.H. Jennings	Physicist	LCP, NIDDK
	A.R. Schultz	Chief, Processor Design	CSL, DCRT
	D.C. Carpenter	Electronics Engineer	CSL, DCRT
	J.T. Morris	Programmer	Systex, Inc.

COOPERATING UNITS *(if any)*

LAB/BRANCH
Computer Systems Laboratory

SECTION
Processor Design Section

INSTITUTE AND LOCATION
DCRT, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL	OTHER
2.0	2.0	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

An integrated laboratory data acquisition and processing system has been developed for LCP and LMB, NIDDK, in Building 2, NIH. The system is configured with satellites coupled through a local network to a host processor. Each satellite is a dedicated microcomputer system performing data acquisition from, and control over, an instrument/experiment. Although acquired data files may be stored locally, they are normally transferred via the network to a host storage medium. The local network allows the host storage medium to appear as a 'virtual' storage device to the satellites.

GPO 914-918

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CT00065-07 CSL

PERIOD COVERED

October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Medical Information Technology Project

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	S.I. Allen	Medical Research Analyst	CSL, DCRT
	C.S. Brown	Consulting Dermatologist	
	R.S. Johannes	Gastroenterologist	Johns Hopkins Univ.
	J.E. Sullivan	Electronics Engineer	CSL, DCRT
	P.S. Plexico	Chief, Project Devel. Sect.	CSL, DCRT

COOPERATING UNITS *(if any)*

LAB/BRANCH

Computer Systems Laboratory

SECTION

Project Development Section

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS	PROFESSIONAL	OTHER
1.2	1.2	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project's goal is to develop better ways to let physicians and their associates use computers in health care recordkeeping for research and patient care. The methodology focuses on providing disease-specific and problem-specific protocols and hierarchies of information that allow rapid convergence on relevant diagnoses, treatments, tests, and procedures.

In past years, computer programs were developed for the physician to produce pharmacy prescriptions and drug-related patient information using high-speed menu selection methods. Later, new modules to aid in producing diagnostic schedules and treatment reports were developed. All these programs run on a personal computer (PC), and several PC's may be linked together in a Local Area Network for clinics or practices needing more than one workstation.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CT00066-07 PSL

PERIOD COVERED

October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Computerized Typesetting of Scientific Papers

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

N. Crawford, PSL, DCRT
M. McNeel, PSL, DCRT; V. A. Parsegian, Ph.D., PSL, DCRT; Science Press; Rockefeller University Press; Biophysical Society; Biophysical Discussions

COOPERATING UNITS *(if any)*

LAB/BRANCH

Physical Sciences Laboratory

SECTION

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.6	0.3	0.3

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The emphasis of this year's activities has been on improved efficiency in code translation on the IBM PC-AT system. With this development, we will realize the use of personal computers as a central link between text generation on a variety of word processing systems and composition on large professional typesetting systems.

A growing feature of this transfer process is reliance on telephone transfer rather than physical transfer of magnetic disks or tapes.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CT00078-05 OD

PERIOD COVERED

October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 charecters or less. Title must fit on one line between the borders.)*

Electronic Typesetting Methods

PRINCIPAL INVESTIGATOR *(List other professionel personnel below the Principal Investigator.) (Neme, title, laboratory, and institute affiliation)*

PI: Patricia O. Miller Information Officer OD, DCRT

COOPERATING UNITS *(if eny)*

Printing and Reproduction Branch, NIH/OD
Medical Arts Section, NIH/DRS

LAB/BRANCH

Office of the Director

SECTION

Office of Scientific and Technical Communications

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS	PROFESSIONAL:	OTHER:
0.1	0.1	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project, begun in FY81, involves collecting and encoding text on magnetic tape for typeSetting by GPO. Eliminating rekeying by a typesetter, and thus the galley proof stage of production, has cut typesetting costs 80 percent.

This year, we worked with an NIH consortium to investigate desk-top publishing methods for NIH; attending demonstrations of MBI, PC/RT, ITEK, and Xerox equipment, as well as the TYPE-X trade show.

Medical Arts installed a typesetting system capable of working from floppy disks. Our test of a PC-created floppy failed on this system, which works well with all types of non-PC word processing diskettes. The only successful input was achieved through an optical character recognition scan of hard copy.

A generic coding scheme was announced this year by the National Information Standards Organization; with the help of GPO, our codes should one day be converted to these methods, to fit a more universal format.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 CT00080-06 CSL

PERIOD COVERED

October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Computer Analysis of Gel Electrophoresis

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	B.L. Trus	Research Chemist	CSL, DCRT
	Gretchen Schieber	Staff Fellow	LSB, NIDDK

COOPERATING UNITS *(if any)*

LAB/BRANCH

Computer Systems Laboratory

SECTION

Systems Design Section

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.1	0.1	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The goal of this project is to allow NIH scientists to easily and accurately quantitate one- and two-dimensional gels. New software has been developed to utilize the features of the image processing facility and to more easily and quickly analyze gels, autoradiographs, and data from hybridization experiments.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CT00081-06 CSL

PERIOD COVERED

October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Rehabilitation Medicine Department Computer System

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	R.L. Martino	Electronics Engineer	CSL, DCRT
	D.C. Carpenter	Electronics Engineer	CSL, DCRT
	N.L. Gerber	Chief, Rehab. Medicine Dept.	RM, CC
	S.J. Stanhope	Expert, Biomechanical Engr.	RM, CC
	M.O. Jarret	Expert, Biomechanical Engr.	RM, CC
	G.C. Hunt	Phys. Therapy Research Coord.	RM, CC
	A. Novick	Staff Physical Therapist	RM, CC

COOPERATING UNITS *(if any)*

LAB/BRANCH

Computer Systems Laboratory

SECTION

Project Development System

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER
0.25	0.25	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project involves the development of computer techniques in collaboration with the Department of Rehabilitation Medicine of the NIH Clinical Center. An Automated Biomechanics Laboratory System that provides methods for the quantitative analysis of human motion has been installed with a combination of purchased instrumentation and computer hardware and software. The instrumentation includes six motion cameras with infrared light sources that are used to acquire the spatial coordinates of anatomical points on the patient's body with reflective markers, two force platforms that are used to measure patient ground reaction forces, and hardwired and telemetry electromyogram acquisition hardware that is used to measure patient muscle activity. This instrumentation is connected to a computer system that performs the necessary data acquisition, calibration, processing, display, and storage functions.

The Automated Biomechanics Laboratory System is now in full operation supporting a number of clinical studies. Two example studies are (1) an evaluation of the effect a modified ankle/foot orthosis has on general gait parameters, ankle and knee motion, and the forces generated at the ankle and knee joints with patients that have hindfoot pain and (2) an investigation of the physiology of postural disturbances in patients with Parkinson's Disease. During the past year activities continued with the development of laboratory instrumentation and the enhancement of the computer system that supports the laboratory's functions. A video system with three standard television cameras and five video cassette recorders that can record the video image from these television cameras and any two of the six measurement cameras was installed in order to provide a record for post-test visual observations. There are no plans for further CSL development on this project beyond FY86.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 CT00082-06 CSL

PERIOD COVERED
October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Image Processing of Electron Micrographs

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	B.L. Trus	Research Chemist	CSL, DCRT
	A.C. Steven	Chief, Struct. Biology Sect.	LCDB, NIDDK
	P.M. Steinert	Visiting Scientist	DB, DCBD, NCI
	T.A. Simpson	Computer Clerk	CSL, DCRT
	R.J. Podolsky	Chief	LPB, NIAMS
	M. Unser	Visiting Scientist	BEIB, DRS

COOPERATING UNITS *(if any)*

LAB/BRANCH
Computer Systems Laboratory

SECTION
Systems Design Section

INSTITUTE AND LOCATION
DCRT, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL	OTHER
0.5	0.5	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project facilitates structure determination from electron microscopy. Suitable software, hardware, and scientific expertise has been provided to allow other scientists, primarily at NIH, to use image processing and computer reconstruction to determine or understand a specimen's structure. Types of data analyzed include intermediate filaments, thin sections of frozen hydrated myofilament of skeletal muscle, and fimbriae of bordetella pertussis.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 CT00090-05 CSL

PERIOD COVERED

October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Molecular Graphics, Computer Modeling, and Sequence Analysis

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	B.L. Trus	Research Chemist	CSL, DCRT
	A.C. Steven	Chief, Struct. Biology Sect.	LCDB, NIDDK
	P.M. Steinert	Visiting Scientist	DB, DCBD, NCI
	B.N. Manjula	Rockefeller University	
	S. Havlin	Visiting Scientist	PSL, DCRT
	G.H. Weiss	Chief	PSL, DCRT
	R. Nossal	Research Physicist	PSL, DCRT

COOPERATING UNITS *(if any)*

LAB/BRANCH

Computer Systems Laboratory

SECTION

Systems Design Section

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.2	0.2	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The sequence of some regular proteins, when correlated with other structural information, such as data from x-ray diffraction, fiber diffraction, electron microscopy, and spectroscopic analysis, can be used to evaluate models of protein or polymer structure. Three current studies involve the sequence analysis of keratin and other intermediate filaments (with NIDDK, NCI); sequence analysis of streptococcal proteins (with Rockefeller University); and computer models of branched polymers (with PSL, DCRT).

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CT00092-05 CSL

PERIOD COVERED

October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Virus Structure As Determined By Image Processing of Electron Micrographs

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	B.L. Trus	Research Chemist	CSL, DCRT
	A.C. Steven	Chief, Struct. Biology Sect.	LCDB, NIDDK
	D. Thomas	Visiting Scientist	LCDB, NIDDK
	M. Unser	Visiting Scientist	BEIB, DRS
	T. Pun	Visiting Scientist	BEIB, DRS

COOPERATING UNITS *(if any)*

LAB/BRANCH

Computer Systems Laboratory

SECTION

Systems Design Section

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.3	0.3	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Two new virus structures have been completed using image processing techniques developed in this laboratory. The high resolution structure of the herpes simplex virus has been determined (with NIDDK and USUHS). In addition, tail fibers of bacteriophage T7 have been analyzed (with NIDDK, NCI, and Brookhaven National Laboratory). These analyses have been successful in part as a result of new software that has been developed for correlation averaging of single particles (with BEIB and NIDDK).

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 CT00098-05 LAS

PERIOD COVERED
October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less Title must fit on one line between the borders.)*
Computer-Based Monitoring of the CNS in Critically Ill Patients

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

R.C. Burgess	Senior Staff Fellow	LAS	DCRT
E.C. Jacobs	Senior Staff Fellow	LAS	DCRT
W.D. Hoffman	Medical Staff Fellow	LAS	DCRT

COOPERATING UNITS *(if any)*
Critical Care Medicine, Clinical Center

LAB/BRANCH
Laboratory of Applied Studies

SECTION
Medical Applications Section

INSTITUTE AND LOCATION
DCRT, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
3.00	2.75	0.25

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Evaluation of the integrity and function of the central nervous system in critically ill patients who are comatose or who have some alteration of mental status currently cannot be done in an ongoing fashion. The purpose of this project is to develop and clinically test a computer-based system for acquisition, analysis, and display of scalp recorded neuroelectric signals (electroencephalogram and evoked potentials). This tool will be used to investigate the degree of dysfunction in neurologically impaired patients, to correlate the indices developed with other measures of cerebral function, and to evaluate the effectiveness of various therapeutic interventions.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 CT00099-05 CSL

PERIOD COVERED

October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 charecters or less. Title must fit on one line between the borders)*

Automated Management of Critically Ill Patients

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	K.M. Kempner	Electronics Engineer	CSL, DCRT
	J.E. Parrillo	Chief, Crit. Care Med. Dept.	CCM, CC
	N. DeClaris	Prof., Schools of Engr., Med.	Univ. of MD

COOPERATING UNITS *(if any)*

LAB/BRANCH

Computer Systems Laboratory

SECTION

Systems Design Section

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.2	0.2	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This research project is concerned with a systems approach to the management of critically ill patients in a clinical setting. Particularly interesting and important problems involve cardiovascular disorders that give rise to low output syndrome. Effective therapy principally involves the administration of one or more fluids and/or drugs in a critical care unit environment.

In order to accomplish the goal of developing systems capable of assisting in the medical management of a critically ill patient on a closed-loop basis, it will be necessary to develop validated models. A state variable approach is utilized in the mathematical modeling of pertinent pharmacokinetic and physiologic processes. This includes three principal subsystems: Pharmacokinetics, Drug/Receptor Interactions, and Cardiovascular Dynamics. Program output includes recommendations for therapy as well as predicted pre- and post-intervention physiologic data values.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CT00105-04 CSL

PERIOD COVERED

October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Medical Image Data Compression

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	H. Sabrin	Electronics Engineer	CSL, DCRT
	D. Syed	Chief, Systems Design Section	CSL, DCRT
	R. Martino	Electronics Engineer	CSL, DCRT
	B.S. Garra	Staff Radiologist	DR, CC

COOPERATING UNITS *(if any)*

LAB/BRANCH

Computer Systems Laboratory

SECTION

Processor Design Section

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER
0.0	0.0	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project is concerned with the minimization of the number of information carrying units used to represent a medical image in order to improve the efficiency of transmission and storage of such images. Various image data compression techniques and their application to medical images have been evaluated to determine the amount of compression attained and the quality of the reconstructed image.

Recently, there has been an increase in the number of medical imaging techniques that result in a digital image representation. These techniques include computed tomography, ultrasonography, magnetic resonance imaging, and digital radiography. As a result of this increased number of digital images, there is a need for Picture Archive and Communication Systems (PACS) that are capable of storing, transmitting, and displaying such images. Because the quantities of image data are large, it is important to consider techniques for data compression to reduce archival and transmission requirements.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CT00108-04 PSL

PERIOD COVERED

October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Studies on the Effect of Solvent Around Biological Macromolecules

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

B. Lee, Ph.D., Expert, PSL, DCRT
D. Lipman, Ph.D., NIADDK; R. Pastor, Ph.D., FDA

COOPERATING UNITS *(if any)*

LAB/BRANCH

Physical Sciences Laboratory

SECTION

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.6	0.5	0.1

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Ever since Dr. C. Anfinsen's pioneering work, it has been the fondest hope of many protein physical chemists to be able to predict the three-dimensional structure of a globular protein from its amino acid sequence. One of the major properties of the amino acids that are used towards this goal is their hydrophobicity. However, the extent to which the hydrophobicity properties of amino acid residues can aid in predicting the structure has not been quantitatively measured. In the past year, Dr. D. Lipman of the Arthritis Institute, Dr. R. Pastor of the FDA and I made a general study of the relationship between the hydrophobicity pattern and an important structural property--the accessibility of individual amino acid residues. Using crystal structures and the native and randomly shuffled sequence data sets, we found that we could indeed quantitatively measure the power of the hydrophobicity pattern in predicting the accessibility pattern of globular proteins. We have found, unfortunately, that there is a severe limitation in the amount of structural information one can extract from the hydrophobicity pattern represented by the native sequence data, implying that even rudimentary structure prediction must include considerations other than hydrophobicity alone.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CT00111-04 LSM

PERIOD COVERED

October 1, 1985 through September 30, 1986.

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Nonparametric Statistics

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)

Gregory Campbell Senior Staff Fellow LSM DCRT

COOPERATING UNITS *(if any)*

LAB/BRANCH

Laboratory of Statistical and Mathematical Methodology

SECTION

Statistical Methodology Section

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, Maryland 20892

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
0.6	0.6	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Research in nonparametric statistics with applications to biomedicine continued. A paper with J. H. Skillings on nonparametric multiple comparisons has appeared. A large-sample theory for weighted U-statistics has been developed and applied to a biomedical project, and confirmed with a computer simulation. The study of the estimation of a paired difference in the presence of randomly missing data is being developed.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CT00119-03 PSL

PERIOD COVERED

October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Membrane Fusion

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

Joshua J. Zimmerberg, M.D., Ph.D., PSL, DCRT
J. Liu, Ph.D., Harvard College, Cambridge, MA; V. A. Parsegian, Ph.D., PSL, DCRT; R. P. Rand, Ph.D., Brock Univ., Canada; B. Trus, Ph.D., CSL, DCRT; M. Whitaker, Ph.D., Univ. College London, England

COOPERATING UNITS *(if any)*

LAB/BRANCH

Physical Sciences Laboratory

SECTION

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.5	1.5	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Submembrane granular fusion to cell membranes appears to be driven by granular osmotic pressure, leading to vesicular swelling and membrane merger at the contact between granular vesicle and cell membrane. We have performed experiments to learn how this swelling is accomplished. Compromising the integrity of the granule membrane to the extent of allowing the passage of small molecules does not affect fusion. Exocytosis proceeds without ions. Polymers prevent exocytosis by preventing the disposal of the granule contents once fusion has occurred. It seems that calcium, in triggering exocytosis, triggers some alteration in the state of the internal granule phase to increase the affinity of this phase for water.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CT00120-03 LSM

PERIOD COVERED

October 1, 1985 through September 30, 1986.

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Computer Graphics and Mathematical Applications

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*

(Name, title, laboratory, and institute affiliation)

K. R. Bhutani Guest Worker LSM DCRT

COOPERATING UNITS *(if any)*

LAB/BRANCH

Laboratory of Statistical and Mathematical Methodology

SECTION

Biomathematics and Computer Science Section

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, Maryland 20892

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
0.2	0.2	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The major objective is to formulate mathematical and computational techniques, and to apply them to problems of biomedical research and computer science.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 CT00121-03 LAS

PERIOD COVERED
October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Applications of Personal Computers to Laboratory Research

PRINCIPAL INVESTIGATOR *(List other professional personnal below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

M.R. Horton	Computer Systems Analyst	LAS	DCRT
R.C. Burgess	Senior Staff Fellow	LAS	DCRT
M.A. Douglas	Computer Systems Analyst	LAS	DCRT
J.E. Fletcher	Chief, Applied Math, Sec.	LAS	DCRT
R.I. Shrager	Research Mathematician	LAS	DCRT
E.C. Jacobs	Senior Staff Fellow	LAS	DCRT

COOPERATING UNITS *(if any)*

Personal Workstation Office (DCRT/OD)

LAB/BRANCH
Laboratory of Applied Studies

SECTION
Medical Applications Section

INSTITUTE AND LOCATION
DCRT, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.30	1.00	0.30

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The goals of this project are to determine the applicability of personal computer-based systems in research laboratories, to assemble such systems, and to test them in laboratory investigations. Because the technological advances in microcomputer architecture are occurring so rapidly, the peripheral equipment and software needed for laboratory applications continue to appear on the market in explosive fashion. The evaluation and selection of available, useful equipment and software for the development of microcomputer-based laboratory systems are undertaken in this project.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CTC0122-03 OD

PERIOD COVERED

October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less Title must fit on one line between the borders.)*

Computerized Typesetting Consultation

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI: Patricia O. Miller Information Officer, OD, DCRT

COOPERATING UNITS *(if any)*

LAB/BRANCH

Office of the Director

SECTION

Office of Scientific and Technical Communications

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.1	0.1	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type Do not exceed the space provided.)*

DCRT techniques for using WYLBUR to prepare text for direct input to computerized typesetting systems have been made available to others in the NIH public affairs community.

Changes this year in the NIH Computer Center's magnetic media affected the methods used to create typesetting drive tapes; the job control language was revised to handle these changes, and new instructions were given to BID's who have used other methods in the past.

Electronic publishing is growing at NIH; this year, NIGMS, NLM, NEI and DLA relied upon our advice.

Continuing assistance was provided to the NIH Editorial Operations Branch, which is typesetting the NIH Scientific Directory/Bibliography via WYLBUR for the first time.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CT00123-03 CSL

PERIOD COVERED

October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Cardiac Ultrasound Image Processing

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	J.M. DeLeo	Computer Systems Analysit	CSL, DCRT
	J.E. Parrillo	Chief, Critical Care Med Dept	CCM, CC
	M.E. Parker	Head, Critical Care Med Dept	CCM, CC

COOPERATING UNITS *(if any)*

LAB/BRANCH

Computer Systems Laboratory

SECTION

Systems Design Section

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS	PROFESSIONAL	OTHER
0.3	0.3	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project was directed towards providing the NIH Clinical Center Medical Intensive Care Unit with the ability to assess cardiac left ventricular function via computer analysis of ultrasound images of the heart. An online system for evaluating left ventricular ejection fraction was developed, tested and installed. This project is now completed.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 CT00124-03 CSL

PERIOD COVERED
October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Personal Computer System for Automatic Coronary Venous Flow Measurements

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI: R.B. Dew	Electronics Engineer	CSL, DCRT
M. Leon, M.D.		NHLBI

COOPERATING UNITS *(if any)*

LAB/BRANCH
Computer Systems Laboratory

SECTION
Project Development Section

INSTITUTE AND LOCATION
DCRT, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS.	PROFESSIONAL	OTHER
0.25	0.25	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects
☐ (a1) Minors
☐ (a2) Interviews
☐ (b) Human tissues
☒ (c) Neither

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

An automated system, based on an IBM PC/XT Personal Computer, was developed to measure coronary artery blood flow during cardiac catheterization.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 CT00128-02 CSL

PERIOD COVERED

October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Urinalysis Data Gathering System

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	J.E. Sullivan	Electronics Engineer	CSL, DCRT
	G. Csako	Senior Staff Fellow	CP, CC
	A. Faust	Systems Analyst	CC
	P.S. Plexico	Chief, Project Development Sect	CSL, DCRT
	M. Rawe	Urinalysis Lab Group Leader	CP, CC

COOPERATING UNITS *(if any)*

LAB/BRANCH

Computer Systems Laboratory

SECTION

Project Development Section

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER
0.5	0.5	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project involves the development of a multiworkstation system for online entry of urinalysis data for the Clinical Pathology Dept., CC. Each workstation is based on an IBM PC-XT and can collect test result data directly from technical personnel or from interfaced instrumentation. Multiple workstations share test results via an Ethernet Local Area Network (ELAN). Each workstation communicates test results to the Clinical Center's Honeywell 716 laboratory computer where the test results are then made available to health care professionals through the Medical Information System. The system was tested and placed in operation during FY86 with two workstations installed in the urinalysis area of the Clinical Chemistry Service. These workstations replace a Mark-Document Reader for sending test results to the laboratory computer.

Test results are currently being entered into the workstations by technicians. Analytical instruments, which perform certain urinalysis tests, and can be interfaced to the workstations, are undergoing accuracy and reliability testing by Clinical Center personnel. One or more of these instruments will be interfaced to the workstations in FY87 if a decision is made to acquire them. Additional urinalysis tests that are not performed at this time may also be incorporated in FY87. Finally, a third workstation may be added in FY87. This workstation would be connected into the existing ELAN.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 CT00129-02 PSL

PERIOD COVERED

October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Membrane Transport

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

Joshua J. Zimmerberg, M.D., Ph.D., PSL, DCRT
F. Bezanilla, Ph.D., UCLA, CA; A. Harris, Ph.D., PSL, DCRT; V. A. Parsegian, Ph.D., PSL, DCRT; A. Walter, Ph.D., LTB, NCI

COOPERATING UNITS *(if any)*

LAB/BRANCH

Physical Sciences Laboratory

SECTION

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.5	1.5	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

To measure the change in internal volume of channels, we have been subjecting perfused preparations to positive and negative osmotic stress. The squid axon K channel volume change inferred from hypertonic stress has an upper bound of about 1,300 cubic angstroms. The mitochondrial voltage-dependent anion channel (VDAC) reconstituted into planar lipid bilayers shows a volume change of 20 to 40 thousand cubic angstroms. These numbers are large if one expects a cork or turnstile mechanism, but are quite reasonable if one imagines a rearrangement involving the entire ionic path.

The gap junction is the locus of direct transfer of ions and small molecules from cell to cell. We are attempting the incorporation of the gap junction channel into an artificial membrane system. Aliquots of the shifted vesicle fractions were added to a bilayer chamber under osmotic conditions known to promote fusion with a planar bilayer. At least three different types of channels were observed. We are presently undertaking steps to fractionate the channels further in order to isolate and identify the junctional channel, and to measure volume changes.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CT00130-02 PSL

PERIOD COVERED

October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Development of Apollo Computer System for Modeling Macromolecules

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

B. Lee, Ph.D., Expert, PSL, DCRT
B. Brooks, Ph.D., OD, DCRT; R. Feldmann, Ph.D., OD, DCRT; R. Pastor, Ph.D., FDA

COOPERATING UNITS *(if any)*

LAB/BRANCH

Physical Sciences Laboratory

SECTION

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.8	0.4	0.2

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A large part of the past year was spent learning the UNIX operating system, the C language, and the Silicon Graphics IRIS workstation. I have now developed a molecular graphics system on the IRIS in C. The system is particularly suited for a realtime manipulation of macromolecules. It is menu-driven so that even an occasional novice user can start using the system without prior preparation. By September 1986, we hope to link this graphics package with the energy minimization--molecular dynamics program that Dr. B. Brooks is developing on the STAR100. Once this linkage is completed, we will have one of the world's most powerful tools for modeling biological macromolecules.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CT00131-02 LSM

PERIOD COVERED

October 1, 1985 through September 30, 1986.

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

DNA Sequence Analysis and Related Methods.

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)

P. Senapathy Visiting Associate LSM DCRT

COOPERATING UNITS *(if any)*

LAB/BRANCH

Laboratory of Statistical and Mathematical Methodology

SECTION

Biomathematics and Computer Science Section

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, Maryland 20892

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
0.7	0.7	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

DNALAB, a comprehensive software package dedicated to aiding recombinant DNA research, has been developed. This package contains, in addition to standard options available in related software, several unique features for sequence analysis. One of the options allows a researcher to identify the restriction enzyme sites closest to a given range of sequence, where the enzymes generate an easily separable fragment that includes the range. Another option enables one to analyze potential splice sites in a gene sequence, delete the hypothetical introns, and analyze the mRNA sequences possible from such splicing.

DEPARTMENT OF HEALTH AND HUMAN SERVICES · PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

Z01 CT00132-02 LSM

PERIOD COVERED
October 1, 1985 through September 30, 1986.

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Algorithms and Other Methods for Biomathematical Computing.

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
J. Pochobradsky Expert LSM DCRT

COOPERATING UNITS *(if any)*

LAB/BRANCH
Laboratory of Statistical and Mathematical Methodology

SECTION
Biomathematics and Computer Science Section

INSTITUTE AND LOCATION
DCRT, NIH, Bethesda, Maryland 20892

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
0.4	0.4	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The major objective of this project is to develop computer algorithms and methods that are useful in biomathematical analysis or display of biomedical data. Implementation of these methods in MLAB is usually under consideration.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CT00133-02 OD

PERIOD COVERED

October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Personal Computer Implementation on Local Area Networks

PRINCIPAL INVESTIGATOR *(List other professionel personnel below the Principal Investigator.) (Neme, title, laboratory, and institute affiliation)*

Robert J. Romanoff	Computer Specialist	PWO,OD DCRT
James S. Del Priore	Mathematician	CSL DCRT
Brian R. Cole	Computer Systems Analyst	DMB DCRT
William L. Risso, Jr.	Electrical Engineer	CSL DCRT
John R. Parks, Jr.	Computer Systems Analyst	DMB DCRT

COOPERATING UNITS *(if eny)*

LAB/BRANCH

Office of the Director

SECTION

Personal Workstation Office

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.5	1.5	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This is a collaborative project between PWO, DMB and CSL to investigate local area network (LAN) technology as it relates to personal computers (PCs), implement PCs on the DCRT Ethernet LAN, and share the knowledge developed with other NIH organizations.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CT00137-02 CSL

PERIOD COVERED

October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Cataract Quantitation Using Image Processing

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	B.L. Trus	Research Scientist	CSL, DCRT
	M. Datiles	Staff Ophthalmologist	NEI, CB
	P. Edwards	Staff Fellow	NEI, CB

COOPERATING UNITS *(if any)*

LAB/BRANCH

Computer Systems Laboratory

SECTION

Systems Design Section

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.1	0.1	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Images produced by the Scheimpflug principle are being used to quantitate eye opacities in a study, whose purpose is to evaluate the potential for the accurate evaluation of changes in cataract patients. This may provide a means of documenting and monitoring cataracts in vivo, allowing clinical trials of drugs that may prevent or reverse the cataract formation process.

Statistical evaluation of our preliminary results is currently underway. In addition, we are considering the viability of using computer clustering methodology for automatic classification or diagnosis of cataracts.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 CT00138-02 CSL

PERIOD COVERED

October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Brain Image Registration

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	K.M. Kempner	Electronics Engineer	CSL, DCRT
	M.V. Green	Physicist	NM, CC
	J.L. Johnson	Research Psychologist	LCS, NIAAA
	D.E. Rio	Medical Physicist	LCS, NIAAA
	J.J. Vucich	Medical Physicist	DR, CC
	J.F. Fessler	Engineering Technician	BEIB, DRS

COOPERATING UNITS *(if any)*

LAB/BRANCH

Computer Systems Laboratory

SECTION

Systems Design Section

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.25	0.25	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

An elusive problem faces researchers involved in the correlation of brain form (structure) from x-ray computed tomography (CT) images and brain function (metabolism) from nuclear medicine positron emission tomography (PET) images. The difficulty concerns the superposition and registration of the tomographic view obtained from these two imaging modalities.

Our approach to this problem is based upon a two-stage solution. First, we are developing a practical method for the accurate and reproducible placement of the head within a tomographic scanner's aperture. Second, we are developing a simplified algorithm for the scaling and registration of digitized images from different scanners, on a digital display subsystem.

The driving force behind the goal of brain image registration is the need to develop a greater understanding of the processes underlying the generation of PET images. It is hoped that development of techniques for the accurate correlation of CT structural data with PET metabolic information will enhance this understanding.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 CT00139-02 CSL

PERIOD COVERED
October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 chrerecters or less. Title must fit on one line between the borders.)*
Advanced Laboratory Workstation

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI: K.E. Gorlen	Electronics Engineer	CSL, DCRT

COOPERATING UNITS *(if any)*

LAB/BRANCH
Computer Systems Laboratory

SECTION
Project Development Section

INSTITUTE AND LOCATION
DCRT, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS	PROFESSIONAL:	OTHER:
0.5	0.5	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The Computer Systems Laboratory is developing an Advanced Laboratory Workstation (ALW), which is a small- to mid-size ($10,000 - $200,000), 32-bit UNIX-based computing engine intended for biomedical research laboratory applications. The project involves the development and integration of a wide variety of software packages into a foundation that can be used by CSL engineers, or NIH bench or clinical scientists to quickly customize an ALW for a particular purpose. We plan to include functions that are valuable in the research laboratory and that state-of-the-art technology makes economically feasible: data acquisition, scientific data processing, data presentation networking data base management, modeling, document preparation, and software development. Our strategy is to acquire the best software that is compatible with the workstation hardware and operating system and integrate it under a user-friendly "desk top" interface: Modern programming techniques such as object-oriented programming will be explored as a means of increasing productivity and software portability.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CT00140-02 CSL

PERIOD COVERED

October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

NIH Campus Area Network

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	W.L. Risso	Electronics Engineer	CSL, DCRT
	R. Fico	Electronics Engineer	CSL, DCRT
	T. Kuhfuss	Electronics Engineer	CSL, DCRT

COOPERATING UNITS *(if any)*

LAB/BRANCH

Computer Systems Laboratory

SECTION

Office of the Chief

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS	PROFESSIONAL	OTHER
3.0	3.0	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The goal of this project is to provide NIH with an assessment of networking requirements on a campus-wide basis, to study available technology, and to recommend appropriate designs to meet the requirements. We have identified applications ranging from video data transmission including images and graphics, to mainframe/microcomputer interconnection, to interconnection among individual local area networks. A concept design for the network is complete, and work is proceeding on technical specifications.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CT00141-02 CSL

PERIOD COVERED

October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Expert Systems in Medicine

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	D. Syed	Chief, Systems Design Sect.	CSL, DCRT
	K.M. Kempner	Electronics Engineer	CSL, DCRT
	H.A. Fredrickson	Electronics Engineer	CSL, DCRT
	J.J. Knight	Computer Systems Analyst	CSL, DCRT
	J.E. Parrillo	Chief, Crit. Care Med. Dept.	CCM, CC
	M.A. Mazer	Medical Staff Fellow	CCM, CC
	G.L. Akin	Critical Care Technician	CCM, CC

COOPERATING UNITS *(if any)*

LAB/BRANCH

Computer Systems Laboratory

SECTION

Systems Design Section

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS	PROFESSIONAL	OTHER
2.0	2.0	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project involves the development of "expert systems" in the medical environment. Expert systems represent feasible applications of artificial intelligence techniques. They are knowledge-based, in that they contain knowledge contributed by experts, and organized, by "knowledge engineers." Generally, they function best in specific, narrowly defined, yet still complex, problem areas. A very important characteristic of these systems is that decisions and recommendations are explained and justified to the user. An initial objective for the project is to develop, in collaboration with the Critical Care Medicine Department of the Clinical Center, a Therapy Advisor Expert System for use in an Intensive Care Unit. The drug administration protocol includes the capability for long-term dose maintenance and eventual dose tapering.

Personal computer based technology (IBM PC-XT or PC-AT) has been utilized in conjunction with commercial expert system shells and an original generated BASIC approach.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CT00142-02 CSL

PERIOD COVERED

October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Retina Metabolism Research System

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	R.L. Tate	Electronics Engineer	CSL, DCRT
	W.F. Hagins, Jr.	Chief, Membrane Biophysics Sec.	LCP, NIDDK
	S. Yoshikami	Research Biologist	LCP, NIDDK

COOPERATING UNITS *(if any)*

LAB/BRANCH

Computer Systems Laboratory

SECTION

Processor Design Section

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS	PROFESSIONAL	OTHER
0.7	0.7	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

For many years CSL has supported retina metabolism research with computer-based systems designed primarily for high-speed data capture and processing. In FY85 CSL installed DAOS (Data Acquisition Operating System), from Laboratory Software Associates of Melbourne, Australia.

The DAOS-interpreted realtime control language provides timing functions, command macros, built-in array operators, virtual data storage, extensibility, and support for a wide variety of popular data acquisition modules. DAOS programs may be written or changed rapidly and easily without the delays imposed by compilation and linking.

DEPARTMENT OF HEALTH AND HUMAN SERVICES · PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CT00143-01 LSM

PERIOD COVERED

October 1, 1985 through September 30, 1986.

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Consulting Services

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)

J. E. Mosimann Chief LSM DCRT

COOPERATING UNITS *(if any)*

J. D. Malley Math. Stat. LSM DCRT
G. Campbell Sr. Staff Fellow LSM DCRT
M. Shapiro Res. Math. LSM DCRT
P. Senapathy Vis. Asso. LSM DCRT
J. Pochobradsky Expert LSM DCRT

LAB/BRANCH

Laboratory of Statistical and Mathematical Methodology

SECTION

Office of the Chief

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, Maryland 20892

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
1.2	1.2	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

LSM staff members provide consulting services in statistics, biomathematics and computer analysis of DNA sequences.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CT00144-01 OD

PERIOD COVERED

October 1, 1985-September 30, 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Personal Computer Bibliographic Systems

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

Ellen M. Chu (DCRT/OD)
E. Cerutti (DRS)
M. Tipperman (DPM)

COOPERATING UNITS *(if any)*

DRS
DPM
DCRT/PWO

LAB/BRANCH

OD

SECTION

DCRT Library

INSTITUTE AND LOCATION

DCRT Building 12A, Room 3018

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.1	0.1	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The project continues advisory and consultative services to NIH staff seeking automation of personal and laboratory bibliographic files for research and publication. Personal computer packages for storage, retrieval, and reformatting were evaluated for DCRT/PWO. These included: JLOG, PRO-CITE, REFERENCE MANAGER, and SCI-MATE. Three systems were selected for a demonstration day co-sponsored by the DCRT Library, NIH Library, and User Resource Center. All provided for (1) data entry from downloaded online searches, as well as manual data entry, (2) database module for retrieval and maintenance, and (3) reformatting citations for a variety of publishers' style requirements.

Future plans: Continuing assistance and investigation of personal computer bibliographic systems for personal and laboratory files.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CT00145-01 OD

PERIOD COVERED

October 1, 1985-September 30, 1986

TITLE OF PROJECT *(80 characters or less Title must fit on one line between the borders)*

Bibliographic Retrieval Systems on Local Area Networks

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

Ellen M. Chu (DCRT/OD)

COOPERATING UNITS *(if any)*

LAB/BRANCH

OD

SECTION

DCRT Library

INSTITUTE AND LOCATION

DCRT Building 12A, Room 3018

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.3	0.3	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type Do not exceed the space provided)*

This project began a year ago, when the DCRT Library joined the initial test stage of the DCRT personal computer implementation on local area networks (lan). Research into network bibliographic retrieval systems for the library catalog included a survey of general purpose database management systems (dbms) and library applications packages. Four dbms and ten packages have been evaluated to date. In the current absence of network systems, we plan a collaborative development project.

A second network application is development of a system for DCRT lan users to access and search data on Library journal holdings and current check-in status of recent issues. Plans for the future include development of a front-end multi-user interface for the serials system.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CT00146-01 OD

PERIOD COVERED

October 1, 1985 to September 31, 1986

TITLE OF PROJECT *(80 characters or less Title must fit on one line between the borders.)*

Understanding Protein Architecture through Simulated Unfolding

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

Richard J. Feldmann, OD, DCRT

COOPERATING UNITS *(if any)*

Bernard R. Brooks OD, DCRT
B.K. Lee PSL, DCRT

LAB/BRANCH

Office of the Director

SECTION

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.0	1.0	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Recent progress in sequencing proteins directly from the gene structure rather than by step by step degradation techniques has exponentially increased the number of available protein sequences. Where crystal structures for members of a protein family exist suitable computer graphic models can be constructed. It is with few exceptions impossible to build a model directly from the amino acid sequence. This is true because in general we do not understand how proteins fold. The understanding of the folding of a protein into a compact three-dimensional structure after synthesis by the ribosome has been slow to develop.

In order to be able to develop a mental picture of the entire structure of the protein, we first developed a graphical sample of protein strucutre. Using CHARMM (Chemistry at Harvard Molecular Mechanics) and the array processor, we were able to represent the backbone of a protein as a smooth, wire-like object. With this procedure we have processed all the protein data sets in the Protein Data Bank from the Brookhaven National Laboratory.

In order to make these results understandable to a wider scientific audience, we have prepared a package of slides for distribution.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CT00147-01 PSL

PERIOD COVERED

October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Cell Membrane Studies

PRINCIPAL INVESTIGATOR *(List other professional personnal below the Principal Investigator) (Name, title, laboratory, and institute affiliation)*

Joshua J. Zimmerberg, M.D., Ph.D., PSL, DCRT
M. Brodwick, Ph.D., Univ. of Texas, TX; F. S. Cohen, Ph.D., Rush Medical College, IL; M. Curran, Univ. of Texas, TX; A. Marty, Ecole Normale Superieure, France

COOPERATING UNITS *(if any)*

LAB/BRANCH

Physical Sciences Laboratory

SECTION

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.5	1.5	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standerd unreduced type. Do not exceed the space provided.)*

Often responses of cells studied with the tight-seal whole-cell recording technique differ from those of intact cells and change with time. We have developed an instrumental array capable of simultaneous physiologic and anatomic realtime measurements of living cells with control of the internal millieu, first using it to measure the capacitance of secretory cells. We have devised a method for purification of mast cells. Large capacitance changes are seen at the instant of secretion in mast cells, consistent with the calculated area of the secretory granule.

We also applied the cell activating compound acetylcholine to a variety of rat lacrymal gland cells to measure the liberation of intracellular calcium. We conclude that there is a loss of a diffusible factor that acts after muscarinic receptor binding and before polyphosphoinositol release. Techniques are currently being developed to prevent the loss of such factors.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 CT00148-01 CSL

PERIOD COVERED
October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Neuromagnetometer Computer System

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	R.L. Martino	Electronics Engineer	CSL, DCRT
	L.D. Nadel	Electronics Engineer	CSL, DCRT
	J.E. Sullivan	Electronics Engineer	CSL, DCRT
	S. Sato	Chief, EEG Laboratory	Off. of Clin. Dir.,NINCDS
	D.F. Rose	Medical Staff Fellow	Off. of Clin. Dir.,NINCDS
	R.J. Porter	Chief, Med. Neuro. Br.	MNB, NINCDS
	P.D. Smith	Physicist	BEIB, DRS
	W.S. Friauf	Chief, Electrical and Electronic Engineer	BEIB, DRS

COOPERATING UNITS *(if any)*

LAB/BRANCH
Computer Systems Laboratory

SECTION
Project Development Section

INSTITUTE AND LOCATION
DCRT, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS	PROFESSIONAL	OTHER
1.5	1.5	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The Medical Neurology Branch of NINCDS, the Biomedical Engineering and Instrumentation Branch of DRS, and the Computer Systems Laboratory of DCRT are collaborating on a research project to noninvasively localize epileptic discharge sources within the human brain utilizing neuromagnetic recording in conjunction with conventional electroencephalogram (EEG) recording.

Many patients with seizure disorders exhibit low-level cellular discharges between seizures, indicated by interictal spikes in their EEG and magnetoencephalogram (MEG) recordings. This project involves the development of computer techniques for automating and enhancing the procedure that is presently used by NINCDS neurologists for determining the intracranial locations of the sources of interictal spikes in patients with epilepsy.

The required MEG and EEG signals are acquired with a system that was purchased from Biomagnetic Technologies, Inc. (BTi) and placed in operation during FY86. This system includes a seven-channel SQUID (superconducting quantum interference device) for measuring the MEG signal from seven sites on the head simultaneously, a combined BTi and Hewlett-Packard (HP) data acquisition system for acquiring the EEG and MEG signals, and an HP 9000 computer workstation for signal processing and graphical display functions.

CSL designed and built a 32-channel signal selection and conditioning interface that was added to the data acquisition system. Methods are presently being developed to automate the real time detection of interictal spikes from the EEG and MEG signals and the extraction of relevant features characterizing the detected waveforms. The information obtained from these features will be used with values extracted from the raw waveforms to generate the graphical displays needed to determine the epileptic foci.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 CT00149-01 CSL

PERIOD COVERED
October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Expert System Techniques

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	D. Syed	Chief, Systems Design	CSL, DCRT
	J.M. DeLeo	Computer Systems Analyst	CSL, DCRT
	J.J. Knight	Computer Programmer	CSL, DCRT

COOPERATING UNITS *(if any)*

LAB/BRANCH
Computer Systems Laboratory

SECTION
Systems Design Section

INSTITUTE AND LOCATION
DCRT, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS	PROFESSIONAL	OTHER
.10	.10	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This activity concerns knowledge sharing among members of the CSL System Design Section who are actively working on expert systems. Informal talks and group discussions on topics of common interest are held. Talks have been given on frames, fuzzy reasoning and Ex-Sys. A two-day intensive brain-storming workshop with an outside artificial intelligence consultant was held. Methods for targeting suitable expert system projects within the NIH scientific community are being discussed.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 CT00150-01 CSL

PERIOD COVERED
October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Nuclear Medicine Computer System

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	H. Ostrow	Electronics Engineer	CSL, DCRT
	S. Bacharach	Physicist	NM, CC
	D. Carpenter	Electronics Engineer	CSL, DCRT
	S. Larson	Chief, Nuclear Medicine	NM, CC
	M. Green	Physicist	NM, CC
	M. Feldman	Computer Programmer	NM, CC

COOPERATING UNITS *(if any)*

LAB/BRANCH
Computer Systems Laboratory

SECTION
Processor Design Section

INSTITUTE AND LOCATION
DCRT, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS	PROFESSIONAL	OTHER
2.0	2.0	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

CSL has continued its support of the Nuclear Medicine Department by assessing their changing and expanding processing needs and translating these into computer requirements that are anticipated to grow 10- to 30-fold over the next few years. This year Nuclear Medicine installed two multislice Positron emission tomography (PET) systems for a total of three, and added a third single photon emission computed tomography (SPECT) system. Nuclear Medicine now has brought online two in-house cyclotrons for generating various isotopes for PET systems.

Last year a Request for Proposals (RFP) for a department-wide computer system was released. This year a contract was negotiated and signed to provide data processing capabilities for both the routine clinical activities and a multitude of research projects. The initial system was installed, which consisted of data acquisition systems (DAS's) that are connected via a network to a large host system. The DAS's will be used for acquisition and processing of routine clinical studies and the host will eventually be used for central storage and display and will provide the computer processing capabilities needed for the research activities.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CT00151-01 CSL

PERIOD COVERED

October 1, 1985 to September 30, 1986

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Audiology ABR Analysis and Interpretation Expert System

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	J.M. DeLeo	Computer Systems Analyst	CSL, DCRT
	A. Pikus	Chief, Audiology Clinic	CC, OD
	A.M. Grimes	Audiologist	CC, OD

COOPERATING UNITS *(if any)*

LAB/BRANCH

Computer Systems Laboratory

SECTION

Systems Design Section

INSTITUTE AND LOCATION

DCRT, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS	PROFESSIONAL	OTHER
0.6	0.7	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project is directed toward developing an expert system that analyzes and interprets Audiologic Auditory Brain Stem Response signals.

1986 Annual Report

Division of Computer Research and Technology

U.S. DEPARTMENT OF HEALTH
AND HUMAN SERVICES
Public Health Service
National Institutes of Health

DCRT

Division of Computer Research and Technology
National Institutes of Health
Bethesda, Maryland 20892

The **Division of Computer Research and Technology** (DCRT) has primary responsibility for incorporating the power of modern computers into the biomedical programs and administrative procedures of NIH. DCRT serves as a scientific and technological resource for other parts of the Public Health Service, and for other Federal organizations with biomedical and statistical computing needs.

DCRT programs focus on three primary activities: conducting research, developing computer systems, and providing computer facilities.

The **Computer Systems Laboratory** provides consultation and collaboration in the design and implementation of specialized computer systems for laboratory and clinical applications.

The **Laboratory of Applied Studies** relates mathematics, statistics, and computer sciences to such biomedical problems as ECG analysis, evaluation of physiological systems in health and disease, and estimation problems in laboratory medicine.

The **Laboratory of Statistical and Mathematical Methodology** provides statistical and mathematical help in the computer analysis of biomedical data and offers statistical and mathematical packages for users.

The **Physical Sciences Laboratory** conducts research in mathematical theory and practical instrumentation to explain biological phenomena in terms of chemistry and physics at the subcellular molecular levels.

The **Computer Center Branch** designs, implements, and operates the NIH Computer Center and provides assistance, training and technical communications to its nearly 17,000 users.

The **Data Management Branch** serves as a central systems analysis, design, and programming resource for data processing projects relating to scientific, technical, management, and administrative data.

The **Office of the Director** provides overall program and management direction for DCRT, and serves as the central NIH focus for automated data processing policy. In addition, the Office sponsors research and development work in molecular and cellular graphics.

The work of DCRT greatly enhances the productivity and creativity of scientific enterprise throughout the National Institutes of Health. Computing has become a vital part of that enterprise.

The DCRT's research, collaborative and service activities have been effectively and broadly incorporated within the conduct and management of the NIH Research Programs. The DCRT was able to meet what were determined to be the critical needs of the NIH community through the individual or combined efforts of the Division's Laboratories, Branches and the Office of the Director.

The Personal Workstation Office, Office of the Director, has been instrumental in extending microcomputer-based office technology in the laboratories, clinics and most of management. The effort has been directed toward support of selected hardware/software configurations that will ensure communications compatibility among different machines, and in particular, communication with the large, central computer facility mainframes.

The molecular graphics project, Office of the Director, has progressed well during this past year. The vision of a local computer network having sufficient arithmetic, graphics and archival capacity to support a team of physical scientist research workers who are attempting to simulate and/or model molecular structure has become a reality. The network consists of about twenty-five computers, which at anytime can be configured into several networks of computers so that the machines may communicate with one another on demand. Each type of computer has been developed in terms of hardware and software to do one or more specific functions as part of the solution to the very complex physical chemical problems in biomedical research.

This project has been the keystone in the DCRT leadership's attempt to define, implement and demonstrate a real-life computer model from which the NIH can plan, with some confidence, for the future of computing at the NIH. Briefly described, the real-world model for computing now at the NIH consists of:

1. A large central computer facility capable of supporting in a variety of applications, a large community of online users drawn from the laboratories, clinics and administrative offices and that is capable of communication with the peripheral computers that are in the scientific and management settings on the one hand and with offsite machines that are part of a larger national or international network. The Computer Center Branch has implemented and operates just such a central computer facility.
2. A number of minicomputer installations that for the most part stand alone for use in a dedicated mode in the laboratories.
3. A substantial number of microcomputers that tend to use highly standardized software that can be used in a very versatile manner, e.g., in an independent mode, in a local linkage with other instruments including another computer as a dumb special purpose terminal for use with the central facility or as an intelligent terminal for use with a large, shared central facility.
4. A number of special purpose computers, each designed to do at least one (more if feasible) necessary task efficiently and swiftly. An example is the Star Technology array processor used in the Molecular Graphics Network that has the processor speed of approximately 1.5-2.0 times that of the supercomputer. In addition, the processor can be attached on demand to a number of front-end computers. Special purpose machines for a variety of tasks can be forseen, for example, image processing in the clinics.

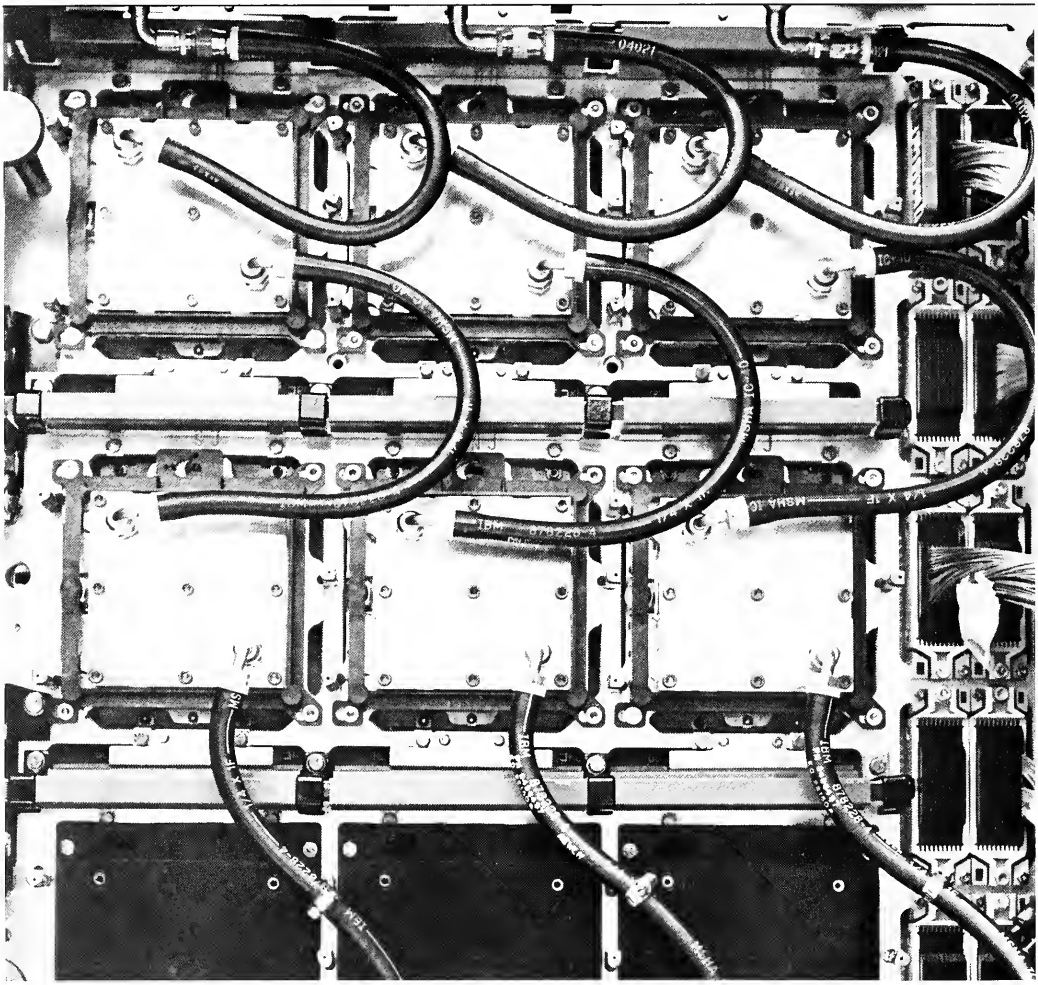
It is constructive to emphasize that this computing capability now exists at the NIH. The constellation of machines and computer programs can be altered, replaced or added to as needs and resources dictate and technical progress allows. The individual components can be arranged in networks of the organization's choice and can provide significant economies for those who are willing to share resources.

All of the DCRT staff can join in the sense of pride that comes from being part of our accomplishments during Fiscal Year 1986.

Arnold W. Pratt, M.D.
Director
Division of Computer Research and Technology

Contents

The new Vector Facility provides the capability for very high-speed scientific computation. This allows extensive computations—such as those needed for studies of molecular structure and dynamics, effects of structural changes, or x-ray crystallographic analyses—that might require weeks of computation on standard laboratory computing equipment, to be completed in a short time.



Computer Center Branch

Joseph D. Naughton, Chief

The Computer Center Branch--the largest component of DCRT--designs, implements, operates, and maintains the NIH Central Computer Utility and its associated telecommunication facilities. The NIH Computer Utility provides timesharing, data base, graphics, batch processing, and word processing services to over 17,000 authorized users.

As a Federal Data Processing Center, the NIH Computer Center also provides data processing services to authorized users in 26 agencies throughout the Federal Government. The Computer Center receives no appropriated funds from Congress, and all services of the NIH Computer Utility are performed exclusively on a fee-for-service, cost-recovery basis.

The NIH Computer Utility consists of two interconnected multicomputer facilities designed around large-scale IBM and DEC mainframe processors. The facilities are linked together by high-speed telecommunication lines, and are connected by telephone lines to thousands of interactive terminals and microcomputers and 268 remote job entry (RJE) computers throughout the United States.

The IBM facility is designed around six IBM 3090 processors with a total of over 384 million bytes of directly addressable memory. The peripheral complex includes 474 online disk drives with a total storage capacity of over 500 billion bytes; 2 mass storage units with a combined capacity of 401 billion bytes; 99 cartridge tape drives with a transfer rate of 3MB/second; 30 tape drives, 24 with 790KB/second, and 6 with 200KB/second transfer rates; 7 page printers at 18,000 lines-per-minute and 5 at 1,100 lines-per-minute, 2 1,000-card-per-minute card reader/punches, and 13 telecommunications controllers supporting a teleprocessing network with over 1,400 lines.

The DECsystem-10 facility is designed around 4 (3 KL10 and 1 KS10) processors with 3,000,000 words of main memory; 12 554-megabyte disk drives and 19 197-megabyte disk drives; 7 780KB/second tape drives and 3 200KB/second tape drives; and 11 communications processors capable of supporting over 50 simultaneous timesharing users.

Ancillary equipment includes 2 computer output microfiche units and film processors, 2 4-color high-resolution plotters, and miscellaneous other devices.

An extensive array of software has been designed and implemented by Computer Center personnel or acquired from other sources and adapted to meet the unique needs of the NIH user community. Three interactive programming systems (DECsystem-10 timesharing, TSO, and WYLBUR) and two large interactive data base management systems (IMS and DB2) are available through the NIH Computer Utility.

Programming languages include FORTRAN, COBOL, PL/1, BASIC, Assembly Language, and SAIL. A variety of statistical analysis, modeling, and utility programs are available, as well as the TELL-A-GRAF, POSTER, and OMNIGRAPH interactive graphics packages for generating graphic output on paper or microfiche.

Over 85 percent of all interactive commands are executed with subsecond response time. Six classes of batch jobs (1 small, 2 medium, 1 large, and 2 vector) provide respective turnaround times of less than 30 minutes, 1 hour, 2 hours, and overnight.

A highly specialized staff of professional, technical, and management personnel ensure smooth functioning of the NIH Computer Utility 24 hours a day, 7 days a week. A staff of computer systems programmers and analysts develop and maintain operating systems software, provide technical consultation on program design and problem resolution, teach training courses, and write technical documentation describing the effective use of the Utility. Computer systems technicians and operations personnel operate and maintain the Computer Utility's hardware and telecommunications networks, and a staff of data entry personnel provide data conversion services. Systems design and management professionals develop long-term program goals and maintain the design integrity of the Utility.

The Computer Center also conducts a number of research and development projects to increase the effectiveness of computer usage in modern biomedical research. Ongoing research projects include development of enhanced output services to permit

high-quality display mathematics, effective transfer of data files between a host and personal computers, and advanced data migration techniques.

FY86 Highlights: Vector Facility, DB2

Scientific computing at NIH took a giant step forward this year as the IBM 3090 Vector Facility was integrated into the NIH Computer Utility. The new Vector Facility provides the capability for very high-speed scientific computation. This allows extensive computations--such as those needed for studies of molecular structure and dynamics, effects of structural changes, or x-ray crystallographic analyses--that might require weeks of computation on standard laboratory computing equipment, to be completed in a short time. The Vector Facility extends the standard instruction to include 63 new instructions, which permit both logical and arithmetic operations on groups of elements (e.g., vectors) with a single instruction.

Because of the unique requirements of NIH users and the Computer Center's experience with scientific computation, IBM asked the Computer Center and a group of NIH researchers to participate in a collaborative project to evaluate and test the hardware and software of the Vector Facility before it was made generally available. In return for their participation in the evaluation project, NIH researchers were given free use of the 3090 processor for performing these types of scientific computations for research activities. Over 500 hours of vector CPU time were used by researchers participating in the testing program. During this time, one researcher reported accomplishing the equivalent of one year's calculations in only one week. The advance testing of the Vector Facility demonstrated the reliability of the hardware and permitted early resolution of the problems that were encountered.

In December, Database 2 (DB2), an entirely new relational data base management system, was made available to users of the NIH Computer Utility. DB2, an IBM product, combines ease-of-use, improved productivity, and user-friendliness with state-of-the-art function, performance, and technology.

DB2 utilizes a simple but powerful high-level data language, Structured Query Language, a nonprocedural language that permits complex data bases to be designed, modified, and easily queried by the end users. DB2 allows users to create their own data base management applications without learning traditional computer languages, such as FORTRAN or COBOL. It permits users who are not professional computer programmers to collect, organize, and analyze data and to reproduce reports customized to their own unique requirements.

Initial response to DB2 was overwhelming. Four sessions each of two new training courses, *DB2 Overview* and *Getting Started with DB2*filled up only a few days after they were announced, and four additional sessions of each of the orientation courses had to be scheduled. Within the first four months of operation, over 250 users had attended the two presentations and the PAL Unit had answered numerous users' questions through the telephone consulting service and the PTR (Programmer Trouble Report) mechanism. The Technical Information Office had mailed over 120 copies of the *DB2 Introductory Set,* a general description of the features and capabilities of DB2, and over 100 copies of the *DB2 Basic Set,* documentation needed for implementing DB2 applications.

DB2 has already undergone a number of enhancements. Several NIH-developed enhancements provided an easy way to create tables and to print reports and move DB2 data tables to disk datasets for analysis with other software such as SAS, TELL-A-GRAF, or WYLBUR. The smooth implementation of DB2 Release 2 provided numerous performance improvements and some functional enhancements.

Communications Networks Improve Availability

Collaboration between scientists at widely separated locations became more practical this year as the services of the NIH Computer Utility became available through two international public communications networks. Users outside the metropolitan Washington

area can now access the interactive services of the Utility through the TYMNET network; and the BITNET network permits scientists and educators to share information.

TYMNET, the world's largest data network, has special communications processors in hundreds of cities across the country that allow users to access the NIH Computer Utility through a local telephone call. The TYMNET network has 10,000 public access telephone ports throughout the country, with local connections in more than 550 U.S. metropolitan areas. TYMNET also provides international access among 63 countries through interconnections with five International Record Carriers.

Hundreds of users of the NIH Computer Utility located outside the Washington metropolitan area have been taking advantage of TYMNET, accessing the network from all over the United States. TYMNET offers significant cost savings over long-distance telephone access; and, since error-correcting protocols are used throughout most of the network, far fewer transmission errors.

The NIH Computer Utility has also joined the BITNET international network, a digital communications network connecting over 1200 computers in universities and other educational institutions and research organizations. The connection to BITNET includes access to computers on the European and Canadian international networks. BITNET allows scientists and educators to exchange messages, mail, and files or documents easily.

IBM System Modernization Completed

The total modernization of the IBM facility was completed late this year, as the sixth and last IBM 3090 Processor Complex was installed on the NIH Computer Utility. The conversion from IBM 3081 processors to IBM 3090 processors began last October when the first 3090 was installed. The 3090 offers twice the execution speed and number of channels as the older IBM 3081 and has an internal design capable of processing 30 million instructions per second. An Expanded Storage System not available in the 3081 provides up to 128 million additional bytes of storage, giving the 3090 six times the amount of main memory as in the 3081.

The IBM 3480 Magnetic Tape Subsystem was implemented on the NIH Computer Utility, and users are reaping the benefits of its increased speed and reliability. The conversion began with a thorough review of tape use by Computer Utility users, followed by consolidation and elimination of unneccessary tapes. The actual transfer of data from the old 10.5-inch open reels to the new compact, enclosed cartridges was completed late in the year. Over 90,000 reels of tape were converted to the new cartridges during the tape upgrade.

All existing 3380 disk storage devices have been converted to new 3380 model AE4/BE4 double density disk drives, which offer improved performance, reliability, and expansion capability. The same physical size as the older model but containing twice as many cylinders, the new disk drive doubled data storage capacity to 568 billion bytes with no increase in floor space or power consumption.

Rate Reductions Offered

The NIH Computer Center celebrated the beginning of fiscal year 1986 by granting users of the NIH Computer Utility significant rate reductions for a wide range of services. Connect time rates were reduced 33.3 percent for both the IBM 3090 and DECsystem-10 facilities, from $1.50 to $1.00 per hour. The editing charge for WYLBUR was reduced 16.7 percent to $.60 per second, and TSO CPU charges were cut 25 percent from $1.00 to $.75 per second.

Rates for online disk space were also lowered. The public DASD rate of $.020 per track-day was reduced 15 percent to $.017 per-track day, and the dedicated DASD rate of $.011 per track-day was reduced 9 percent to $.01 per track-day.

Users of the NIH DECsystem-10 services also received substantial rate reductions. In addition to the 33 percent reduction in connect time charges, the charge for online disk storage space on the DECsystem-10

was reduced 20 percent to $.064 per 100 blocks per day. Processing charges for users of the DECsystem-10 were reduced in two ways. The cost per machine unit was reduced 17.5 percent to $.61 per machine unit and the billing algorithm itself was restructured, giving the effect of an additional rate reduction of 16 percent per typical timesharing session.

Monthly lease charges for 3270-type display terminals and printers provided by the Computer Center were also decreased an average of 16 percent. Users of dedicated Remote Job Entry service received a large rate reduction when its charge was reduced a full 50 percent from 0.00 to .00 per month. An opportunity for further economy for RJE users was instituted later in the year as newer software made it possible for the Computer Center to charge only for the amount of RJE service actually used by switched RJE workstations.

Hardware and Software Enhancements

New state-of-the-art modems capable of sending and receiving data at 30, 120, and 240 characters per second were made available this year. This enables users with terminals capable of transmitting at 240 characters per second to use that speed.

The VTAM SNA/SDLC communications facilities, which support both dedicated and dial-in synchronous 3270-type terminals and personal computers on the IBM System 370, were expanded this year when the number of 4800 bps dial-up ports was increased and a new level of service, 2400 bps synchronous dial-up service, was offered. This new service opened the VTAM network to many new users, especially those with personal computers.

A significant increase in virtual storage was made available for both TSO sessions and batch jobs on the IBM System 370 facility. The REGION size limit was increased to 6144K, or six million bytes, an increase of more than fifty percent over the previous limit of 4000K. Efficient handling of virtual storage in MVS/XA decreases the overhead for very large regions; therefore, region use over 4000K is charged at only 5 percent of the regular rate.

The Virtual Storage Access Method (VSAM) and its companion utility program AMS (ACCESS Method Services) moved into production state this year, after nearly a year of testing. VSAM offers many advantages over the older access methods, and is expected to eventually replace ISAM (Indexed Sequential Access Method). Electronic Spread Sheet (ESS) software package became available for use with IBM 3270-compatible terminals under TSO. With ESS, the user can use spreadsheets to summarize and display budgets, forecasts, cost/benefit analyses, projections, evaluation, and comparisons. Easy-to-learn and use, the ESS package includes a tutorial, user reference material, and an online HELP facility.

Two software packages were retired this year. SPEAKEASY was eliminated because of declining usage, and SPSS was retired and replaced with the newer SPSS-X.

Training

The Computer Center continued to meet training needs through a variety of formats, including classroom training, computer-assisted learning, and self-study materials.

Two new courses, *TELL-A-GRAF* and *Laboratory Data Acquisition (with the PC),* were added to the Computer Center's Training Schedule and one of the more popular courses, *SAS,* was revised. The *TELL-A-GRAF* course taught users to create pie charts and bar charts and enhance these charts using special TELL-A-GRAF features. The course involved three days of lecture and two days of hands-on experience using a Tektronix terminal. *Laboratory Data Acquisition*, a four session hands-on course, was designed to assist students in analyzing and meeting laboratory data acquisition needs with an IBM PC-based system. The revised *SAS* course enabled beginning level students to begin using SAS after one week of instruction.

The Training Unit received more requests for classroom courses than it could accommodate; nevertheless, 86

percent of all on-time and eligible applications were accepted. This year 3,721 requests for training were received and 2,785 students were accepted into 143 sessions of 51 different courses.

The Computer Center's very popular Assisted by Computer (ABC) Independent Training Facility added two new courses this year. *Introduction to Program Logic* introduced potential programmers and other interested persons to the basic principles of program design and logic. *Multiple ACTIVE Files* showed WYLBUR users how to increase WYLBUR's versatility by taking advantage of the multiple active files available. This brought the number of ABC courses to six, along with *Introduction to WYLBUR, WYLBUR SET Commands and Profile, Computer Literacy,* and *Introduction to Job Control Language.* More than 5,900 people took advantage of the opportunity to learn at a terminal, in privacy and at their own speed and convenience during FY86.

A new self-study tool, *ISPF Dialog Management Services,* was made available to enable users to create interactive applications, which will run under the Interactive System Productivity Facility (ISPF) and its companion product, the Program Development Facility (PDF). Designed for students who have a background in TSO or a programming language and are familiar with ISPF/PDF, the course consists of three textbooks, a workbook, and additional reading assignments from corresponding reference manuals.

Customer Assistance and Documentation

Frequent interaction between the user and the Computer Center enhances the success of the Computer Utility. Customer assistance ensures maximum utilization of the Utility's resources and eliminates problems before they start. This year, Computer Center consultants handled 21,450 customer assistance contacts and researched and answered 3,455 Programmer Trouble Reports.

Changes to improve the performance and reliability of the operating system required the implementation of 138 SYSGENS (software reconfigurations). Approximately 16,870 fixes, both preventive and corrective, were tested and applied to the system, and 27 new releases of current software packages were installed.

Documentation is essential to enable users to make effective use of the Computer Utility. A completely new *DECsystem-10 Timesharing Guide* was published this year, as well as an extensively revised *Terminal Operator's Guide.* Extensive documentation was prepared about DB2 to benefit users at every level, and the Computer Center *User's Guide* underwent five updates and revisions. The Automatic Documentation Service was utilized by 7,500 users, and 155,000 copies of technical publications were sent to those users and to individual requesters. There were six new technical documents published and 37 revisions or updates. *INTERFACE,* technical newsletter published periodically by the Computer Center, was issued seven times this year, including the *Annual Index.*

Future Plans

In the coming year, work will begin on developing technical specifications for a Request for Proposals (RFP) to replace and/or upgrade the NIH Computer Utility during the next decade. This will ensure that the NIH Computer Utility remains on the cutting edge of technology and continues to provide the most cost effective service possible in response to constantly changing user demands.

Work will continue on the development of special software and hardware needed to offer research scientists the ability to produce high-quality, publication grade, display mathematics. Advanced file transfer programs are being developed to facilitate the transfer of files and data bases between the Utility's host and the User's PC's. Work will be completed on the implementation of advanced data migration techniques. These new services will take advantage of the capabilities of the new operating systems software (i.e., MVS/XA) and the new equipment installed this past year. The ability of the telecommunication systems to handle a wider variety of terminals and remote computers will be enhanced and a new protocol conversion service will make synchronous applications available from asynchronous terminals.

Peter Munson of the Laboratory of Theoretical and Physical Biology, NICHD, discusses the interpretation of a statistical test with Brian Cole, DMB, as part of the BLOSSOM project to explore ways that personal computers can be used to analyze biomedical data.

Data Management Branch

J. Emmett Ward, Chief

The Data Management Branch (DMB) provides advice and assistance to research investigators, program officials, and administrators throughout NIH in planning for and obtaining computer data processing services. In this role the branch is a central NIH resource for systems analysis, design, and programming. The Branch is also responsible for the development, maintenance, and processing of the NIH Administrative Data Base and the Clinical Center's Clinical Information Utility. There are currently 50 permanent full-time employees whose disciplines include computer science, mathematics, and statistics.

DMB staff design and create computer-based data management systems that provide practical solutions to the unique mix of administrative, scientific, and management data processing problems encountered at NIH. Each new computer system user is provided comprehensive training in all system facilities and functions of the system provided by DMB. In addition DMB staff teach courses about programming tools; provide advice on data management techniques to NIH programmers; serve as consultants to the BID's for obtaining and monitoring contracting services for computer systems development; and create and maintain general purpose, user-oriented programming tools to speed building and improve operation of applications systems.

DMB comprises four sections. **The Applied Systems Programming Section** (ASPS) and the **Scientific Applications Section** (SAS) provide general computer systems analysis and programming services for all of the BID's. The ASPS supports general data management, and the SAS handles those projects that require scientific data analysis.

The **Data Base Applications Section** develops and maintains the central administrative data base for NIH materiel and financial management. The **Clinical Support Section** develops and maintains the Clinical Information Utility as a data base for research and patient care in the Clinical Center.

Broad Involvement in the NIH Mission

The NIH Administrative Data Base (ADB) is an ongoing developmental project that uses data base technology in support of NIH-wide materiel and financial management. Progress to date has seen major improvement in:

1. the control of market and stock requisitioning, central and delegated ordering, receiving, payment procedures and central and self service stores inventories,
2. the elimination of 100 percent of delegated and over 75 percent of central paperwork and paper flow, and
3. the replacement of intermediate data collection procedures by electronic data transfer.

During the past year, pharmacy and glassware inventories were added to the ADB. Cashier functions were also integrated with other payment processes.

We have completed requirements analysis and design, in a new ADB effort to automate the processing of requests for central services. In early Fall, we expect to pilot test the software to support Phase One of this effort. Phase One will include service request entry, estimating, review, and billing.

The moratorium on the development of data base software for financial management is still in effect. This includes budget formulation, fund control, fund certification and general ledger processing. Pending a review of the departmental Financial and Administrative Integrated Management Systems (FAIMS) project, financial management functions will either be included in FAIMS or released for development within the ADB.

The Clinical Information Utility (CIU) is another ongoing effort. It provides a unique archive of integrated data for use in patient care and research. Data from the Clinical Center's Medical Information System and clinical service activities have been integrated and made available for retrieval. During the past year, over 800 requests for clinical information have been satisfied using the CIU.

BRIGHT STAT-PAK is an online computer system designed to run on the DECsystem-10 and to allow clinical investigators to directly perform analysis on their data. Four of the BRIGHT statistical programs were translated into macro programs for use with the LOTUS 1-2-3 spreadsheet programs on a personal computer. These macros (called BLOSSOM) provide support for one- and two-way analysis of variance, error structure analysis, non-linear least-squares curve fitting, and residuals analysis. During its first year, we have provided fifty copies of BLOSSOM to the BID's.

Information on all Federal government-supported human nutrition research and training now is collected and made available to all Federal agencies, to Congress and its staff, and to the scientific community by way of a computer system developed by DMB for the Office of the Director, NIH. This system underwent major modification this year to provide expanded nutrition descriptors and a comprehensive narrative on each research project.

Because of the large number of other projects for which DMB has provided support, it is not reasonable to mention them all. However, some are worth summarizing to give the reader an idea of the breadth of DMB's involvement in the NIH mission. They are as follows:

- **Phoenix Clinical Information System** --provides clinical data base maintenance and analyses support for the Epidemiology and Field Studies Branch of NIADDK.
- **Child Health Information Protocol System** -- manages the NICHD extramural research project portfolio.
- **Weekly Mood Inventory** --supports the seasonal affective disorder study of NIMH based on comparison of a weekly self analysis of mood versus the standard Hamilton Depression Rating Scale (HDRS).
- **Pulmonary Care and Analysis System** --enables immedate analysis of current pulmonary data to support patient care in the NHLBI. It also includes a facility to download data to personal computers so that data can be shared with other organizations.

On several evaluation projects, DMB is providing support for DB2, IBM's relational data base management system, to satisfy the online information requirements of the Office of the Director, NIH, and many of the BID's.

In the area of general support for NIH activites, DMB continued to maintain and teach courses on the Inquiry and Reporting System (IRS) and MARK IV; to maintain and distribute the NCI Survival System; and to consult with and assist NIH programmers and contractors, enabling facile use of DCRT computer facilities.

Potentials for Data Base Management

With the recent introduction of DB2 on the DCRT mainframe, we now have a tool that supports online relational data base retrieval. With some modification, we also have the potential to support full data base management. DMB is collaborating with the Computer Center Branch to define these modifications and to request their implementation by the vendor. If these modifications are implemented, DMB will have a complete set of packages for large and small scale data base management.

When feasible, the use of personal computers (PC's) for data base management, retrieval, and analysis is highly desirable. DMB is examining the feasibility of using data base management for standalone and shared purposes in a Local Area Network. It is clear that as PC speeds improve and networks stabilize, the use of personal computers for shared data base management will become a reality. We will provide an organized approach to using these facilities as soon as they become available.

Facilities for downloading from and uploading to the DCRT mainframe using PC's have been implemented during the past year. However, it is desirable to improve these capabilities by making them more user friendly. DMB will be examining options for improving these functions and, if necessary, will write software to achieve a higher degree of user friendliness.

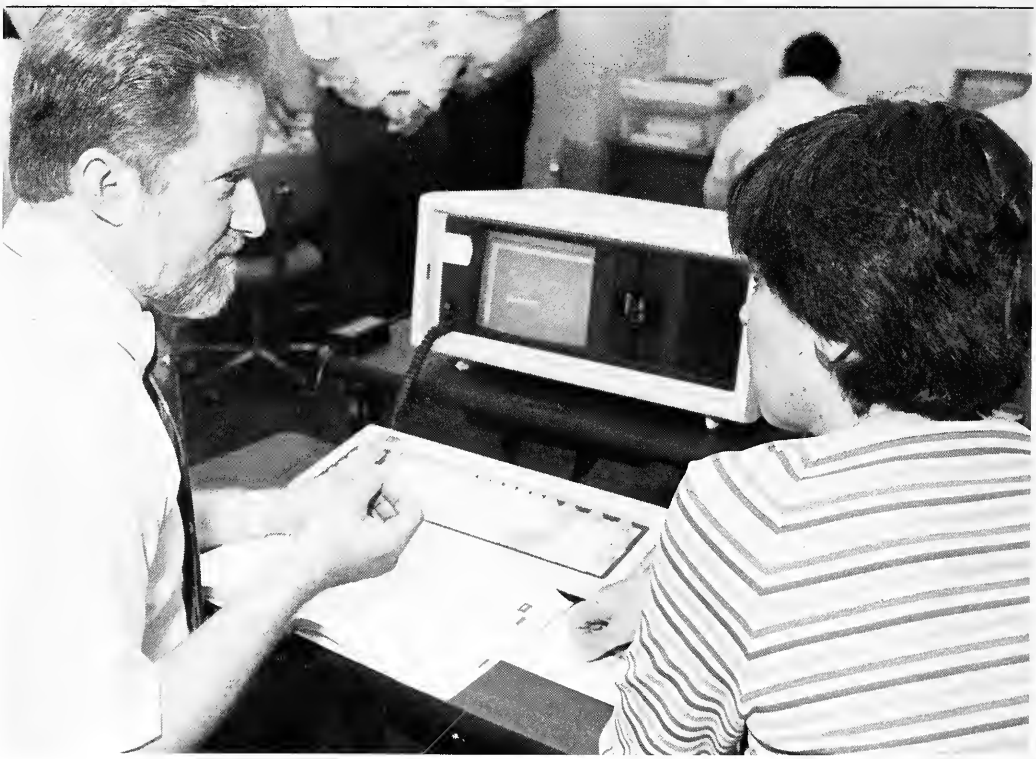
The Computer Center Branch, Personal Workstation Office and DMB are collaborating in an effort to define a universal terminal/personal computer that operates as a standalone PC, is identifiable in a local area network, accesses all mainframe facilities, and emulates a 327X terminal.

Publications

Aubuchon, J.P., and Roberts, G.C.: Computerized Selection of Donors for Inclusion in Red Cell Antibody Panels. *Transfusion* (in press).

Rodbard, D., Munson, P.J., and Cole, B.R.: Linear Regression in Medical Research--The BRIGHT STAT-PACK Approach. *New England Journal of Medicine* , letter to the editor, July 17, 1986, page 198. F0020

CSL collaborates with, or provides support to, NIH investigators whose research requires the use of personal computers in laboratories or clinics. This year, a course was offered on using personal computers for laboratory data acquisition. It covered signal and instrument investigation, analog and digital signals, data collection and storage, and data analysis and display.



Computer Systems Laboratory

Alan M. Demmerle, Chief

The Computer Systems Laboratory (CSL) is composed of 28 individuals with expertise in the disciplines of electronics engineering and computer science and experience in applying these disciplines to the automation of laboratory and clinical research. We concentrate on the development of specialized computer systems to facilitate data collection and analysis from laboratory instruments and from clinical research. The Laboratory's programs include internally generated research and development into new applications of computers to biomedical research; identification of appropriate technology for these applications; and development of systems that benefit communities of users. We also design and implement systems for intramural investigators at NIH who come to us with their problems relating to the automation of their research. This generally involves the purchase of some mini- or microcomputer hardware, and electronic hardware to interface the computer to the instrumentation. It always involves the development of software for these systems; system software to control the automation process, and analysis software to analyze collected data and display results.

Projects vary in size from those requiring only a few man-months to complete, to some taking up to eight man-years. For the most part our projects involve actually implementing computer-based systems, but some involve only consulting services, i.e., the delivery of advice; we implement systems only for intramural programs but we consult for both intramural and extramural programs and occasionally for other agencies. Most projects are accomplished in collaboration with the scientists expecting to use the system; some are done in collaboration with other computer scientists employed in the Institutes. The equipment purchased for these systems is generally paid for by the users' Institutes.

In selecting projects, we are mindful of the leverage of our efforts. We prefer projects that will benefit a large number of people, or have special impact on biomedical research. We hope to find generalized solutions to a large class of problems; the **Advanced Laboratory Workstation** described below is an example. We concentrate on advanced systems that are not commercially available.

Lab Automation, Expert Systems, Networks Highlight Year

This year we worked on 28 projects, most of which were started in previous years. Some of the more important projects are summarized below. Detail on all projects can be found under *Research Projects* at the end of this section.

Flow Cytometry/Cell Sorting: Software for two parameter generalized data analysis has been made available for use by cell sorters at NIH. We also evaluated the use of cluster analysis for multiparameter data.

Rehabilitation Medicine Department Computer System: This system is now in operation supporting clinical studies of gait. This year CSL completed its development work by the installation of a video system for post test visual observations and by further development of some of the laboratory's EMG instrumentation.

Brain Image Registration: A practical method for reproducible placement of the head within a tomographic scanner's aperture was developed. Also, an algorithm is being developed for the scaling and registration of digitized images from different scanners.

Clinical Pathology Urinalysis Data Collection: An IBM PC-based system for online entry of urinalysis data was completed and is now in routine use.

Medical Information Technology: Several IBM PC's operating in a network allow practicing physicians to produce diagnosis-specific treatment schedules. The system is in trial use by a dermatologist in private practice and by a gastroenterology clinic in a university hospital.

Distributed Laboratory Data Acquisition & Control System: Improvements were introduced to several instrument interfaces on this network of instruments. Also, a set of programs for data analysis and graphics display of lab data was completed.

Advanced Laboratory Workstation: Techniques devised at other Computer Science centers for the application of 32-bit computer technology were evaluated for use at NIH for generalized scientific data acquisition, processing and presentation, and for networking and data base management.

NIH Campus-wide Network: Plans are complete for an NIH campus-wide electronic network allowing the interconnection of computers, terminals, and instrument systems. A broadband link now interconnects two buildings; several other buildings will soon be added to the network.

Expert Systems in Medicine: A system for treatment of ICU shock patients sensitive to the time course of events during recovery period has been completed and is being tested. Other areas of application for medical expert systems are being explored.

Image Analysis: Several projects involving analysis of electron micrographs, gel electrophoresis and cataract images were carried out using a VAX 11/780 image analysis system developed here in past years. CSL collaborates with other NIH scientists to analyze their images with our image analysis tools and methods.

Nuclear Medicine Computing: A large multicomputer system to accomodate the imaging requirements of the Nuclear Medicine Department was ordered and delivered this year. Developmental work on the system has begun to build a network for transmission of video and digital data from multimodality images.

Neuromagnetometer Computer System: CSL has added a signal selection and conditioning interface to a SQUID (Superconducting QUantum Interface Device). Other equipment was purchased to facilitate intercranial location of interictal spikes in patients with epilepsy. IBM PC's were added to the system for use in remote display. Severe magnetic noise problems impede progress.

PC Lab Consulting: Advice was offered to numerous laboratory researchers concerning PC system configuration, software packages, and data acquisition techniques. Also, a course was offered on the use of IBM PC's for laboratory data acquisition.

Future Expansion Areas: Networks, Laboratory Workstations, Expert Systems

No major shift in emphasis or type of work is expected next year. Some of the projects reported here will continue into the future. Generally speaking, we will be seeking new ways to use increasingly widespread computing power. Along these lines we expect to expand the campus-wide computer networks, and to expand into other areas where expert systems can relieve scientists of highly complex but recurring analysis and decision-making. We expect to develop the use of computers as managerial decision support systems. We expect to continue and expand our work developing a workstation for use by NIH lab scientists, which combines computing power with data acquisition, display, data management and communication--in short, a complete laboratory computing environment.

CSL is mindful that one of its prime purposes here at NIH is to help biomedical scientists with their data collection analysis and display problems as they arise, as new instruments are created, and new research ideas are born. We remain committed to solve these problems with the ever-changing computer technology.

Publications and Presentations

Allen, S.I., Johannes, R.S., Brown, C.S., Kafonek, D.R., and Plexico, P.S.: Prescription-Writing With A PC. *Proceedings of the Ninth Annual Symposium on Computer Applications in Medicare Care.* pp. 54-59, 1985.

Bunde, A., Havlin, S., Stanley, H.E., Trus, B.L., and Weiss, G.H.: Diffusion In Random Media With A Topological Bias. *Phy. Rev. Letters* (in press).

Carpenter, D.C., and Martino, R.L.: An Analog Signal Interface for a Biomechanics Laboratory. *Proceedings of the 39th Annual Conference on Engineering in Medicine and Biology* (in press).

Collett, B., Gorlen, K., and Podolsky, R.J.: A New Photon-Counting, 2-D X-Ray Detector For Muscle Diffraction. *Biophysical Journal* 49: 473a, 1986.

Datiles, M.B., Edwards, P.A., Trus, B.L., and Green, S.B.: Reproducibility Studies on the Scheimpflug Camera. Presented at Assoc. for Res. in Vision and Ophthalmology Annual Meeting, Sarasota, FL, May, 1986.

Dew, R.B.: Personal Computer System For Automatic Coronary Venous Flow Measurement. Presented at SCAMC, Nov. 10-12, 1985.

Fico, R.: Broadband Cable Plant Design With Spreadsheets Using Ashton-Tates Framework. *Data Communications Magazine* (in press).

Fiori, C., Leapman, R., and Gorlen, K.: Computer-Aided Compositional Mapping in Scanning Electron Column Devices. In Armstrong, J.T. (ed.): *Microbeam Analysis - 1985.* San Francisco, San Francisco Press Inc., 1985, pp. 219-226.

Fraser, R.D.B., and Trus, B.L.: Molecular Mobility in the Gap Regions of Type 1 Collagen Fibrils. *Bioscience Reports* 6(2): 221-226, 1986.

Gershon, N., Porter, K., and Trus, B.: The Cytoplasmic Matrix: Its Volume, Surface Area and the Diffusion of Molecules Through It. *Proc. Nat. Acad. Sci. (USA)* 82: 5030-5034, 1985.

Havlin, S., Trus, B.L., and Weiss, G.H.: A Phase Transition in the Dynamics of an Exact Model for Hopping Transport. *Phys. Rev. Letters* (in press).

Havlin, S., Trus, B.L., and Weiss, G.H.: A Diffusion Model for Transport on Loopless Aggregates. *J. Phys. A.* 18: L1043-L1047, 1985.

Jacobson, P.W., Osborne, J., Tate, R., Wiesenfeld, P., and Gallo, L.L.: Effect of Bile Salts on the Conformation of Rat Pancreas Cholesterol Esterase. Poster Session: Symposium 86, GWU, Wash., D.C., May, 1986.

Leapman, R., Fiori, C., and Gorlen, K.: Elemental Imaging by EELS and EDXS in the Analytical Electron Microscope: Its Relevance to Trace Element Research. *Biological Trace Element Research* (in press).

Manjula, B.N., Acharya, A.S., Mische, S.M., Fairwell, T., Trus, B.L., and Fischetti, V.A.: The Complete Amino Acid Sequence of Streptococcal Pep M5 Protein: Presence of Two Structurally Distinct Domains and Implications to Biological Functions. In Kimura, Y., Kotami, S., and Shiokawa, Y. (Eds.): *Recent Advances in Streptococci and Streptococcal Diseases.* Bershire, England, Reedbooks, Ltd., 1985, pp. 185-187.

Martino, R.L.: The Automated Biomechanics Laboratory at the National Institutes of Health. The First Annual Eastern Gait Laboratories Meeting. Newington, Connecticut, November 8, 1985.

Powell, J.I., Morris, J.T., and Jennings, W.H.: An Integrated Data Analysis and Graphics Program for Spectrographic Data. Pitts. Conf. and Exposition on Analytical Chem. and Applied Spectroscopy, Atlantic City, NJ, March 10-14, 1986.

Pun, T., Steven, A.C., and Trus, B.L.: Augmentation de la Resolution D'Images de Microscope par Techniques Correlatives et Analysis Factorielle. Presentation at Swiss Fed. Inst. of Tech., Lausanne, Switzerland, July 3, 1985.

Sabrin, H.W., and Martino, R.L.: Hadamard Transform Coding of Medical Images. *Proceedings of the 39th Annual Conference on Engineering in Medicine and Biology* (in press).

Sabrin, H.W., and Martino, R.L.: Medical Image Compression With Transform and Huffman Coding. *Proceedings of the Eighth Annual Conference of the IEEE Engineering in Medicine and Biology Society* (in press).

Steven, A.C., Bisher, M.E., Trus, B.L., Thomas, D., Zhang, J.M. and Cowell, J.L.: The Helical Structure of Fimbriae of Bordetella Pertussis. *Journal of Bacteriology* (in press).

Steven, A.C., Hainfeld, J.F., Trus, B.L., Wall, J.S. and Steinert, P.: Radial Organization of Intermediate Filaments Determined by Scanning Transmission Electron Microscopy. *Journal of Cell Biology* 101(5): Pt. 2, 41, 1985.

Steven, A.C., Maizel, J.V., Studier, F.W., Parry, D.A.D., and Trus, B.L.: Tail Fibers of Bateriophage T7; Deduction of the Structure of A Filamentous Recognition Protein From Electron Microscopy and Secondary Structure Prediction. Gordon Conf. on 3D Electron Microscopy of Macromolecules, Antrim, NH, July, 1985.

Steven, A.C., Roberts, C.R., Hay, J., Bisher, M.E., Pun, T., and Trus, B.L.: The Hexavalent Capsomers of Herpes Simplex Virus Type 2: Symmetry, Shape, Dimensions and Oligomeric Status. *Journal of Virology* 57(2): 578-584, 1986.

Steven, A.C., Simpson, T., Trus, B.L., Wall, J.S., Furcinetti, P. and Hainfeld, J.F.: Radial Density of Macromolecular Filaments Determined from Dark-Field Stem Micrographs: Improvements in Technique and Some Applications. Conference on Recent Advances in Electron and Light Imaging in Biology and Medicine, New York Academy of Sci., NY, March, 1986.

Steven, A.C., Simpson, T.A., Trus, B.L., Furcinnitti, P.S., Hainfeld, J.F. and Wall, J.S.: Radial Density Profiles of Macromolecular Filaments Determined for Dark-Field Scanning Transmission Electron Micrographs: Improvements in Technique and Some Applications. NY Acad. of Sciences Conf. on Recent Advances in Electron and Light Imaging in Biology and Medicine (in press).

Steven, A., Stall, R., Steinert, P., and Trus, B.: Computational Straightening of Images of Curved Macromolecular Helices by Cubic Spline Interpolation Facilitates Structural Analysis by Fourier Methods: *Proc. of Symposium on Neural Filaments* (in press).

Steven, A.C., Stall, R., Steinert, P.M., and Trus, B.L.: The Structure of Intermediate Filaments from Electron Microscopy: Potentialities of Computational Straightening of Curved Filaments to Admit Fourier Analysis of Helical Organization. *Symp: Hierarchic Order of Helical Assemblies of Neurofilament Proteins in Normal Neurons and in Brains of Alzheimer Patients* (in press).

Steven, A.C., Trus, B.L., Hainfeld, J.F., Wall, J.S., and Steinert, P.M.: Conformity and Diversity in the Structures of Intermediate Filaments. In: Wang, E., Fischman, D., Kiem, R.K.H., and Sun. T., (Eds.): *Intermediate Filaments.* New York, New York Acad. Sci., 1985, Vol. 455, pp. 371-380.

Steven, A.C., Trus, B.L., Unser, M., McDowell, A.W., Dubochet, J. and Podolsky, R.J.: Myofilament Lattice of Vertebrate Skeletal Muscle Visualized By Correlation Averaging of Frozen Hydrated Thin Sections. Electron Microscopy Society of America, Annual Meeting, Albuquerque, NM, Aug. 10-15, 1985.

Steven, A.C. and Trus, B.L.: The Structure of Bacteriophage T7. In: Harris, J.R., and Hornes, R.W. (Eds.) *Viral Structure, Electron Microscopy of Proteins* London, Academic Press, Vol. 5, 1985, pp. 1-35.

Thomas, D., Newcomb, W.W., Brown, J.C., Wall, J.S., Hainfeld, J.F., Trus, B.L. and Steven, A.C.: Molecular Organization of the Vesicular Stomatitis Virus Determined from Dark-Field Stem Micrographs. *J. Microsc. Spectrosc. Electron.* 10: 499-504, 1985.

Thomas, D., Newcomb, W.W., Brown, J.C., Wall, J.S., Hainfeld, J.F., Trus, B.L. and Steven, A.C.: Molecular Organization of Vesicular Stomatitis: A Scanning Transmission Electron Microscopy Study. Presentation at the Biology of Negatively Stained Viruses, Cambridge, England, Sept., 1985.

Trachtenberg, S., Steinert, P., Trus, B., and Steven, A.: Electron Microscopy and Image Analysis of Paracrystalline Filament Bundles Obtained from Psoriatic Epidermal Keratin. *Proc. of Symposium on Neural Filaments* (in press).

Trus, B.L.: Macromolecular Structures By Computer Image Processing and Electron Microscopy. Biomedical Perspectives on Image Science, Pt. 2, NASA, Goddard Space Flight Center, October, 1985.

Trus, B.L., Podolsky, R.J., Unser, M.I., McDowell, A.W., Dubochet, J., and Steven, A.C.: The Myofilament Lattice of Skeletal Muscle Visualized by Image Processing of Frozen-Hydrated Thin Sections. Annual Poster Meeting, CSEM, May, 1986.

Trus, B.L., Steven, A.C., Unser, M.I., McDowell, A.W., Dubochet, J., and Podolsky, R.J.: Correlation Averaging Techniques To Rectify Disordered Myo-

filament Lattices Visualized in Frozen Hydrated Thin Sections Of Vertebrate Muscle. XIth International Congress On Electron Microscopy, Kyoto, Japan, Aug./Sept., 1985.

Unser, M., Steven, A.C. and Trus, B.L.: Odd Man Out: A Quantitative Objective Procedure for Identifying Anomalous Members of a Set of Noisy Images of Ostensibly Identical Specimens. *Ultramicroscopy* (in press).

Research Projects

Computer Support for Flow Cytometry/Electronic Cell Sorters (FC/ECS)

L.K. BARDEN

with: W. Gandler (DCRT/CSL); S. Sharrow, D. Stephany (NCI/IB).

The FC/ECS project involves designing and implementing computer-based data acquisition, management, and analysis systems for Flow Cytometry applications. Our recent effort has been primarily directed toward high volume sites, which are not adequately supported by commercially available data systems. The Immunology Branch, NCI, is the primary site where prototype hardware and software are installed and tested.

During this fiscal year, the two-parameter expansion of the APR data analysis package (developed by CSL for the DLDACS project) has been integrated into our data management and analysis system. Users of this system now have a coherent, flexible means of applying sophisticated data analysis procedures to histogrammed single and dual parameter data.

The data management and analysis software developed for this project have been incorporated by Becton-Dickinson into an upgrade of their FACS-440/ Consort-40 data systems. This upgrade, called System-80, is available at distribution cost from B-D. One site on campus (Surgery Branch, NCI) has already converted to the new B-D system and another (Arthritis and Rheumatism Branch, NIADDK) is in the process of purchasing the required additional hardware. According to B-D, there are five other Consort-40 sites on campus that could benefit from this upgrade. A B-D FACS II site at the Naval Medical Research Institute is waiting for delivery of required hardware and is scheduled for upgrade to our currently supported full data system sometime this fall.

In response to a need to analyze multiparameter data without first reducing its dimensionality, CSL has begun investigating alternative analysis methods. One promising method is non-hierarchical cluster analysis. A cluster analysis package developed for flow cytometry data by Dr. Robert F. Murphy at Carnegie-Mellon University has been evaluated for possible use at NIH. The evaluation protocol involves comparing data analyzed using APR with results from the cluster analysis program. The increasing complexity of experimental design and the amount of data acquired per sample would benefit from a more advanced data analysis capability.

Cardiac Scintillation Probe

H.G. OSTROW

with: S. Bacharach, Ph.D., M. Green (CC/NM); R. Bonow, M.D., R. Canon, Ph.D. (NHLBI/CB).

The cardiac scintillation probe is a transportable device used to noninvasively monitor left ventricular function. The system uses nuclear medicine ECG-gated scintigraphic techniques and consists of a small detector and microcomputer system mounted on a cart.

The cardiac scintillation probe, when used in conjunction with left ventricular (LV) catheterization, permits simultaneous quantification of the variation of LV volume and pressure allowing parameters such as LV compliance to be continuously monitored. In addition, measurements such as ejection fraction, filling and ejection rates, and temporal relationships can be made.

This year the probe continued to be used in the cardiac catheterization laboratory to assess left ventricular function. One protocol involved patients with hypertrophic cardiomyopathy who are studied pre- and post-operation. The data acquisition and processing is being performed by the Nuclear Medicine Department and Cardiology Branch. CSL is consulting, directing, and assisting in the analysis of the data. One manuscript was published this year and two others are in preparation. The Hewlett-Packard computer system that was purchased last year is presently being used with a scintillation camera in the catheterization laboratory to perform the pressure-volume studies. CSL

worked closely with Nuclear Medicine to provide this pressure-volume capability using the camera.

Continued development of the probe system has been postponed for the present. We are assessing the capabilities of the camera in the catheterization laboratory to determine if further development of the probe using the Hewlett-Packard system is warranted.

Medical Intensive Care Unit Patient Monitoring Computer System

K.M. KEMPNER
with: J.E. Parrillo, M.D., S.L. Huntley (CC/CCM); J.F. Fessler (DRS/BEIB).

The Medical Intensive Care Unit (MICU), administered by the Critical Care Medicine Department in the NIH Clinical Center, receives critically ill patients from clinical programs of NIH. The research goals of this project include the development of techniques for automated patient monitoring and noninvasive measurements of the cardiovascular and respiratory systems. In addition, catheterization studies are performed as necessary to obtain data that are available only through invasive methodology.

Working with Clinical Center staff, CSL contributed to the engineering design of the intensive care unit. CSL also undertook the specification, procurement, and installation of the bedside patient monitoring equipment and six computer systems:

1. a Patient Data Management Subsystem for automated patient monitoring and online data entry/storage/retrieval;
2. a Vascular Research Subsystem for acquiring and processing cardiovascular data and waveforms during catheterization;
3. a Software Development Subsystem for developing programs for online nuclear medicine and cardiac ultrasound studies;
4. an Ultrasound Imaging Subsystem for the visualization of intracardiac structures;
5. a Pulmonary Function Testing Subsystem for the calculation of respiratory parameters; and
6. Data Analysis and Graphics Subsystems for the correlation of data obtained from the other subsystems, as well as immunology and clinical pathology laboratory data.

The automation of the MICU has aided the medical staff by managing the large amount of data needed for the care of the critically ill patient, performing desired calculations, and allowing measurements that would not otherwise be possible. The multiple-computer system is utilized in support of research protocols, in addition to direct patient care.

During FY86 we have developed plans for the addition of an Ethernet Local Area Network within the Critical Care Medicine Department, to connect the expanding number of IBM PC-XT and -AT personal computer Data Analysis and Graphics Subsystems. This LAN will be utilized for scientific data interchange as well as for administrative purposes. The LAN will be implemented during the next fiscal year along with the installation of several additional IBM personal computer systems.

Rehabilitation Medicine Department Computer System

R.L. MARTINO, Ph.D.
*with:*D.C. Carpenter (DCRT/CSL); N.L. Gerber, M.D., S.J. Stanhope, Ph.D., M.O. Jarret, Ph.D., G.C. Hunt, A. Novick (CC/RM).

This project involves the development of computer techniques in collaboration with the Department of Rehabilitation Medicine of the NIH Clinical Center. An Automated Biomechanics Laboratory System that provides methods for the quantitative analysis of human motion has been installed with a combination of purchased instrumentation and computer hardware and software. The instrumentation includes six motion cameras with infrared light sources that are used to acquire the spatial coordinates of anatomical points on the patient's body using reflective markers, two force platforms to measure patient ground reaction forces, and hardwired and telemetry electromyogram acquisition hardware that measures patient muscle activity. This instrumentation is connected to a computer system that performs the necessary data acquisition, calibration, processing, display, and storage functions. The system is used to evaluate the effectiveness of drug therapy, orthotic and prosthetic

devices, and medical interventions on patients who are amputees, or have arthritic, orthopedic, and neurological conditions.

The Automated Biomechanics Laboratory System is now in full operation supporting a number of clinical studies. Two example studies are:

1. an evaluation of the effect a modified ankle/foot orthosis has on general gait parameters, ankle and keen motion, and the forces generated at the ankle and knee joints in patients who have hindfoot pain; and
2. an investigation of the physiology of postural disturbances in patients with Parkinson's Disease.

During the past year, development of laboratory instrumentation and the enhancement of the computer system continued. A video system with three standard television cameras and five video cassette recorders was installed. The recorders can capture the video images from the television cameras and from any two of the six measurement cameras. The video system provides a record for post-test visual observations.

There are no plans for further CSL development on this project beyond FY86.

Automated Management of Critically Ill Patients

K.M. KEMPNER
with: J.E. Parrillo, M.D. (CC/CCMD); N. DeClaris, Sc.D. (University of Maryland).

This research project is concerned with a systems approach to the management of critically ill patients in a clinical setting. Particularly interesting and important problems involve cardiovascular disorders that give rise to low output syndrome. Effective therapy principally involves the administration of one or more fluids and/or drugs in a critical care unit environment.

In order to accomplish the goal of developing systems capable of assisting in the medical management of a critically ill patient on a closed-loop basis, it will be necessary to develop validated models. A state variable approach is utilized in the mathematical modeling of pertinent pharmacokinetic and physiologic processes. This includes three principal subsystems: Pharmacokinetics, Drug/Receptor Interactions, and Cardiovascular Dynamics. Program output includes recommendations for therapy as well as predicted pre- and post-intervention physiologic data values.

A package of FORTRAN programs for modeling the drug administration protocol, and the three major subsystems accounting for drug action on cardiovascular function, were implemented on the IBM System 370 facility. These programs simulate the intensive care unit environment and the patient's response to the theoretical pharmacologic interventions. The numerical integration procedure, utilized to solve the nonlinear differential equations representing the modeled subsystems, has been enhanced to allow the selection of Predictor-Corrector integration techniques in addition to the Runge-Kutta method.

The use of automated systems in the implementation of therapeutic protocols within a critical care unit adds a new treatment modality. It may be expected to have a significant effect on protocol design for patient care, clinical drug trials, and the study of the etiology and therapy of specific disease entities.

Modifications will be incorporated into the models as necessary to improve system performance. Consideration will be given to the development of techniques for the calibration of the models to patient-specific model parameters.

Brain Image Registration

K.M. KEMPNER
with: M.V. Green (CC/NM); J.L. Johnson, Ph.D., D.E. Rio, Ph.D. (NIAAA/LCS); J.J. Vucich (CC/DR); J.F. Fessler (DRS/BEIB).

An elusive problem faces researchers involved in the correlation of brain form (structure) from x-ray computed tomography (CT) images and brain function (metabolism) from nuclear medicine positron emission tomography (PET) images. The difficulty concerns the superposition and registration of the tomographic view obtained from these two imaging modalities.

Our approach to this problem is based upon a two-stage solution. First, we are developing a practical method for the accurate and reproducible placement of

the head within a tomographic scanner's aperture. Second, we are developing a simplified algorithm for the scaling and registration of digitized images from different scanners, on a digital display subsystem.

Precise orientation of the subject's skull within the scanner's aperture will be monitored and recorded through the use of a Polhemus Navigation Systems position/orientation transduction subsystem connected to an IBM PC-XT. Image processing and display will be performed utilizing the NIAAA imaging system, consisting of a DEC PDP-11/24 minicomputer and a Gould-DeAnza 6400 Image Processor subsystem.

System fabrication has been completed, and experimentation with sensor attachment techniques has resulted in the development of an inexpensive custom-molded oral appliance to allow the position/orientation subsystem's sensor to be fixed to the subject's skull. Approaches to the head immobilization problem are also under investigation.

The driving force behind the goal of brain image registration is the need to develop a greater understanding of the processes underlying the generation of PET images. It is hoped that development of techniques for the accurate correlation of CT structural data with PET metabolic information will enhance this understanding.

Future efforts will center on the development of targeting software that will provide the technician utilizing the system with visual cues necessary for precise and reproducible head placement.

Urinalysis Data Gathering System

J.E. SULLIVAN
with: C. Csako, M.D., M. Rawe (CC/CP); A. Faust (CC/DIR); P.S. Plexico (DCRT/CSL).

This project involves the development of a multiworkstation system for online entry of urinalysis data for the Clinical Pathology Dept., CC. Each workstation is based on an IBM PC-XT and can collect test result data directly from technical personnel or from interfaced instrumentation. Multiple workstations share test results via an Ethernet Local Area Network (ELAN). Each workstation communicates test results to the Clinical Center's Honeywell 716 laboratory computer where the test results are then made available to health care professionals through the Medical Information System. The system was tested and placed in operation during FY86 with two workstations installed in the urinalysis area of the Clinical Chemistry Service. These workstations replace a Mark-Document Reader for sending test results to the laboratory computer.

Test results are currently being entered into the workstations by technicians. Analytical instruments, which perform certain urinalysis tests, and can be interfaced to the workstations, are undergoing accuracy and reliability testing by Clinical Center personnel. One or more of these instruments will be interfaced to the workstations in FY87 if a decision is made to acquire them. Additional urinalysis tests that are not performed at this time also may be incorporated in FY87. Finally, a third workstation may be added in FY87. This workstation would be connected into the existing ELAN.

Medical Information Technology Project

S.I. ALLEN
with: C.S. Brown, M.D. (Bethesda); R.S. Johannes, M.D. (Johns Hopkins University School of Medicine); J.E. Sullivan, P.S. Plexico (DCRT/CSL).

This project's goal is to develop better ways to let physicians and their associates use computers in health care recordkeeping for research and patient care. The methodology focuses on providing disease-specific and problem-specific protocols and hierarchies of information that allow rapid convergence on relevant diagnoses, treatments, tests, and procedures.

In past years, computer programs were developed for the physician to produce pharmacy prescriptions and drug-related patient information using high-speed menu selection methods. Later, new modules to aid in producing diagnostic schedules and treatment reports were developed. All these programs run on a personal computer (PC), and several PC's may be linked together in a Local Area Network for clinics or practices needing more than one workstation.

Pilot studies with a dermatologist (C.S. Brown) and gastroenterologist (R.S. Johannes) are underway involving medical transactions entered directly by the practicing physicians. Initial results with the PC system show more precise and more rapid prescription-writing.

Future plans include introducing a graphic input tool to capture anatomic disease descriptions; simplifying data base management functions to reduce the user's reliance on computer professionals; archiving; and testing physician-operated modules with other ambulatory care specialties.

Cardiac Ultrasound Image Processing

J.M. DELEO
with: J.E. Parrillo, M.D., M.E. Parker, M.D. (CC/CCM).

This project has been directed towards providing the NIH Clinical Center Medical Intensive Care Unit with the ability to assess cardiac left ventricular function via computer analysis of ultrasound images of the heart.

Ultrasound imaging is a highly regarded modality, as it is less invasive than currently popular cineangiography and nuclear imaging methods. Moreover, ultrasound technology has advanced so that fairly sharp images are computer-accessible directly in realtime.

In our approach, cardiac ultrasound images captured on an HP77020A Ultrasound Imaging System are transmitted directly to an HP2100 Computer System from the patient bedside. Left ventricular ejection fractions are computed from end-diastolic and end-systolic ellipsoid volume estimates, which are determined from orthogonal ellipse area measurements. These measurements are made both automatically by an adaptive gray-scale thresholding technique and semi-automatically, by means of ultrasonographer specified boundaries of the left ventricle. Ejection fractions compare well with those obtained by nuclear imaging methods.

For more practical use, computer keyboard access at the patient bedside is necessary but not achievable without substantial recabling within the Care Unit. This is not considered feasible at this time. A simple ejection fraction estimation procedure using elliptical area measurements made directly from the HP Imaging System was devised. It has proven useful and is used routinely.

Molecular Graphics, Computer Modeling, and Sequence Analysis

B.L. TRUS, Ph.D.
with: A.C. Steven, Ph.D. (NIDDK/LCDB); P.M. Steinert, Ph.D. (NCI/DB); B.N. Manjula (Rockefeller University); S. Havlin, Ph.D., G. Weiss, Ph.D., R. Nossal, Ph.D. (DCRT/PSL).

The sequence of some regular proteins, when correlated with other structural information, such as data from x-ray diffraction, fiber diffraction, electron microscopy, and spectroscopic analysis, can be used to evaluate models of protein or polymer structure. Three current studies involve the sequence analysis of keratin and other intermediate filaments (with NIDDK, NCI); sequence analysis of streptococcal proteins (with Rockefeller University); and computer models of branched polymers (with PSL, DCRT).

As the complete sequence of keratin, other intermediate filaments, and other helical proteins becomes available, an analysis of the sequence can proceed by studying periodicities in the sequence, and by computer prediction of the conformational properties of the specific amino acids in local regions of the chain. These predictions can be used to generalize structures where related sequences are available, and to draw conclusions as to similarities and differences.

Standard Fourier methods have been used to analyze the sequences and to cross-correlate sequences. These sequence regularities are usually correlated with structural features, such as the collagen triple helix, the alpha helix, or the tropomyosin double stranded alpha helix. Additional software has been developed at NIH to illustrate correlations and create maps of the linear sequences studied. We have developed other methods of model building to construct models of actin, actin with S1 subunits, microtubules, and simple branched polymers.

This research is significant because many proteins do not form three-dimensional crystalline solids whose

structure can be analyzed by classical x-ray diffraction. However, if these proteins are regular, comparison and analogy with related proteins can be used to model the unknown structures in order to understand the structure and functioning of the proteins. In addition, one can use computer models to analyze possible protein structures based on criterion other than regular periodicities.

This year computer models continue to be useful in studying polymers, percolation clusters, and diffusion in such structures. Analysis of a new streptococcal M protein sequence is in progress. A new look at the structure of collagen in terms of its amino acid sequence has been published. This analysis has been the first to help understand the difference in physical and chemical properties in the gap versus the overlap region of collagen.

As new sequences of regular (helical) proteins become available, it will be relatively easy to model these sequences and describe their structures both graphically and quantitatively.

Virus Structure As Determined by Image Processing of Electron Micrographs

B.L. TRUS, Ph.D.
with: A.C. Steven, Ph.D., D. Thomas (NIDDK/LCDB); J. Hay (USUHS); M. Unser, Ph.D., T. Pun, Ph.D. (BEIB).

Two new virus structures have been completed using image processing techniques developed in this laboratory. The high resolution structure of the herpes simplex virus has been determined (with NIDDK and USUHS). In addition, tail fibers of bacteriophage T7 have been analyzed (with NIDDK, NCI, and Brookhaven National Laboratory). These analyses have been successful in part as a result of new software that has been developed for correlation averaging of single particles (with BEIB and NIDDK).

The electron micrographs were taken with a Philips EM400T microscope and the Brookhaven STEM. Some micrographs were preselected by optical diffraction. Negatives were digitized on a Perkin-Elmer 1010MG microdensitometer and analyzed by means of the PIC computer system. Results were photowritten on the Perkin-Elmer microdensitometer. Images were processed using software developed primarily at NIH.

This year we have continued to study and publish results on the structure of Vesicular Stomatitus Virus. In addition, correlation averaging has been used to elucidate the structure of capsomers of Herpes Simplex Virus Type II. Finally, a review chapter detailing the structure of Bacteriophage T7 has been published.

Viruses are significantly smaller than bacteria, and as a result are not seen in a light microscope. Information about their structure comes from electron microscopy, which is limited by resolution, low contrast, and noise. If staining is used, the resolution is limited by the size of the stain and often noise as a result of uneven staining. However, because virus structures are generally periodic or contain some symmetry, they are perfect candidates for image processing. This project should be considered as basic research aimed at increasing understanding of the structure and functions of viruses in general, as well as of subclasses of viruses similar to those studied to date.

We anticipate evaluating other viruses for suitability for examination with these methods, and continuing with this ongoing project to determine the structure of various classes of viruses.

Image Processing of Electron Micrographs

B.L. TRUS, Ph.D.
with: A.C. Steven, Ph.D. (NIDDK/LCBD); P.M. Steinert, Ph.D. (NCI/DB); M. Unser, Ph.D. (BEIB/DRS), T.A. Simpson (DCRT/CSL); R.J. Podolsky, Ph.D. (NIAMS/LPB).

This project facilitates structure determination from electron microscopy. Suitable software, hardware, and scientific expertise has been provided to allow other scientists, primarily at NIH, to use image processing and computer reconstruction to determine or understand a specimen's structure. Types of data analyzed include intermediate filaments, thin sections of frozen hydrated myofilament of skeletal muscle, and fimbriae of bordetella pertussis.

The micrographs were taken with a Philips EM400T microscope and the Brookhaven STEM. Some

micrographs were preselected by optical diffraction. Negatives were digitized on a Perkin-Elmer 1010MG microdensitometer and analyzed by means of the PIC computer system. Results were photowritten on the Perkin-Elmer microdensitometer. Images were processed using software developed primarily at NIH.

The major success of this year has been the analysis of frozen-hydrated thin sections of myofilament lattice from vertebrate muscle. Substantial new software was necessary to correct for compression, nonlinearity of the contrast of the transfer function, as well as other difficulties. The results of our analysis is being evaluated. One new procedure has been the development of statistical criteria for accepting or rejecting images based on mutual consistancy. Additional effort has also been made in developing new software for processing STEM data. Also, the helixal structure of fimbriae from bordetella pertussis has been determined.

Computer analysis of electron micrographs is still a relatively recent addition to the tools available to scientists for structural analysis. Few laboratories have the combined software and hardware capability to perform the image processing and image reconstruction available at NIH. These techniques are especially powerful when applied to two-dimensional crystalline structures. In addition, we can correlate and align similar particles that are not crystalline, and correct for a number of artifacts and experimental problems.

This project will continue software development as needed. In addition, as new biological structures become available for analysis, these will be examined.

Computer Analysis of Gel Electrophoresis

B.L. TRUS, Ph.D.
with: L. Leive, Ph.D. (NIDDK/LCBG); T. Pun, Ph.D. (DRS/BEIB); G. Schieber, Ph.D. (NIDDK, LSB).

The goal of this project is to allow NIH scientists to easily and accurately quantitate one- and two-dimensional gels. New software has been developed to utilize the features of the image processing facility and to more easily and quickly analyze gels, autoradiographs, and data from hybridization experiments.

Wet gels are rephotographed onto Ektapan 4162 black and white film. The black and white negative (4162 or an autoradiograph) is scanned on the Perkin-Elmer 1010MG microdensitometer and stored on disk for later processing. Software to process these images was developed primarily at NIH.

This project has produced many useful results to a number of scientists at NIH in FY86. New methodology currently has been developed in collaboration with BEIB to automatically and quickly analyze 1-D gels. This procedure automatically locates lanes, subtracts background, and integrates the total content across each lane. The results are depicted graphically, and a printout is produced that includes a summary and simple plot.

Use of gel electropheresis and autoradiographs is commonplace in chemical, biochemical, and biomedical research. However, the quantitation of these gels is difficult. We have developed systems that accurately and easily provide this quantitation to the scientist.

Options are being added to the software to provide additional flexibility to the research scientist. A video camera has been procured to provide more rapid digitization of gels. Evaluation of video input is currently under investigation.

Cataract Quantitation Using Image Processing

B.L. TRUS, Ph.D.
with: M. Datiles, P. Edwards, M.D. (NEI/CB).

Images produced by the Scheimpflug principle are being used to quantitate eye opacities in a study, whose purpose is to evaluate the potential for the accurate evaluation of changes in cataract patients. This may provide a means of documenting and monitoring cataracts in vivo, allowing clinical trials of drugs that may prevent or reverse the cataract formation process.

Statistical evaluation of our preliminary results is currently underway. In addition, we are considering the viability of using computer clustering methodology for automatic classification or diagnosis of cataracts.

Pharmaceuticals are available that may prevent or reverse the cataract formation process. A clinical trial in human patients cannot be pursued because of inadequate means of documenting and monitoring cataracts in vivo. It is hoped that this methodology will provide the statistical and image processing foundation to document and assess changes in lens opacities in cataract patients.

In addition, we hope to be able to use a video camera for quicker data acquisition.

Distributed Laboratory Data Acquisition and Control System

J.I. POWELL
with: D.C. Carpenter (DCRT/CSL); J.T. Morris (Systex, Inc.); W.J. Jennings (NIDDK/LCP).

D-LDACS is an integrated approach to providing data acquisition, archiving, and processing of laboratory data for the two laboratories of NIDDK in building 2. D-LDACS is configured with satellite microcomputers independently controlling and acquiring data from an instrument/experiment. A Local Area Network couples the satellites to a host processor.

Instruments connected to the network include: a Cary 118, Cary 210, Cary 219, and two Perkin-Elmer 580B spectrophotometers; a microspectrophotometer (fabricated by NIDDK); a Jasco J500A spectropolarimeter; a Varian ESR spectrometer; an EG&G Raman SPEC spectrometer; a RAMALOG spectrometer and a retinal stimulus response experiment. A data analysis and graphics program, APR, was developed for the host to provide for automated processing of large volumes of laboratory data while maintaining a simple, user friendly interface for interactive use. Data analysis using APR may be performed remotely from graphics terminals located throughout the building. A presentation on APR was made at the 1986 Pittsburgh conference.

The RAMALOG LDACS was completed this year and improvements to the C118, C210 and C219 LDACS are in progress. D-LDACS is nearly complete and represents an essential resource for many research projects in building 2. The utilization of the PDP 11/70 is approaching the capacity of that system.

Consideration is being given to the best means of adding additional computing capacity. A scheduled move to building 5 in 1988 is an opportunity to upgrade the system with more recent networking technology.

Medical Image Data Compression

H. SABRIN
with: D. Syed, R. Martino, Ph.D. (DCRT/CSL); B.S. Garra, M.D. (CC/DR).

This project is concerned with the minimization of the number of information carrying units used to represent a medical image in order to improve the efficiency of transmission and storage of such images. Various image data compression techniques and their application to medical images have been evaluated to determine the amount of compression attained and the quality of the reconstructed image.

Recently, there has been an increase in the number of medical imaging techniques that result in a digital image representation. These techniques include computed tomography, ultrasonography, magnetic resonance imaging, and digital radiography. As a result of this increased number of digital images, there is a need for Picture Archive and Communication Systems (PACS) that are capable of storing, transmitting, and displaying such images. Because the quantities of image data are large, it is important to consider techniques for data compression to reduce archival and transmission requirements.

Progress in FY86 was limited to reporting the results attained during the previous year.

The techniques developed should benefit any medical center that needs to store and transmit a large number of medical images.

With the departure of the principal investigator, support for this project has ceased.

Integrated Input/Output

J.S. DEL PRIORE
with: R. Pilgrim (DCRT/DMB); D. Songco (DCRT/PWO); P.S. Plexico (DCRT/CSL).

This project expands the user interface of a personal computer from the usual keyboard input and CRT display to include more friendly and efficient methods of communication. In the past, CSL efforts on this project have focused on the development and modification of hardware and software to support desirable interface features like speech recognition and voice response, bar code interpretation, touch-sensitive CRT screens, and graphics input devices.

A Multiple Input Computer Key demonstration system (MICKEY) had been developed utilizing the above mentioned I/O. This system has demonstrated the feasibility of monitoring multiple inputs simultaneously, letting the user choose the method most appropriate to the particular situation.

Aside from the demonstration aspects of the system, development in FY86 has been restricted to incorporating the voice components for use by a DCRT/DMB computer programmer who is quadriplegic. The use of voice recognition and voice response has substantially improved his ability to communicate with computer facilities like the DCRT central systems by using an IBM PC as an intermediary.

Future work on this project will continue to focus on evaluating new devices as they become available.

Retina Metabolism Research System

RAMON L. TATE, Ph.D.
with: W.F. Hagins, Jr., M.D., Ph.d., S. Yoshikami, Ph.D. (NIDDK/LCP).

For many years CSL has supported retina metabolism research with computer-based systems designed primarily for high-speed data capture and processing. In FY85 CSL installed DAOS (Data Acquisition Operating System), from Laboratory Software Associates of Melbourne, Australia.

The DAOS-interpreted realtime control language provides timing functions, command macros, built-in array operators, virtual data storage, extensibility, and support for a wide variety of popular data acquisition modules. DAOS programs may be written or changed rapidly and easily without the delays imposed by compilation and linking.

In support of special hardware required for timing and stepping motor control, DAOS was extended in FY86 with added software modules. These extensions to DAOS are used for the positioning of a neutral density filter and for the generation of complex synchronous timing sequences. A series of command macros also have been written to simplify the process of experimental protocol setup and to make the data file format compatible with the LDACS system.

Dr. Hagins has adapted a recently developed dual parameter detector for use in the study of isolated retina metabolism. This detector combines a microcalorimeter with a very sensitive electrical activity sensor. Planning is underway for revision of the data acquisition module to support simultaneous data acquisition from multiple ADC boards for use with this detector. Enhancement and correction of the documentation is also planned.

Advanced Laboratory Workstation

K. GORLEN
with: P. Plexico, J. Powell, R. Dew (DCRT/CSL).

The Computer Systems Laboratory is developing an Advanced Laboratory Workstation (ALW), which is a small to mid-size (K- 0K), 32-bit, UNIX-based computing system intended for biomedical research laboratory applications. The project involves the development and integration of a wide variety of software packages into a foundation that can be used by CSL engineers, or NIH bench or clinical scientists, to quickly customize an ALW for a particular purpose. We plan to concentrate on providing functions such as data acquisition, scientific data processing, data presentation, networking, data base management, modeling, document preparation, and software development. By emphasizing portable software based on UNIX and C and the use of standards, we hope to support workstations from a variety of manufacturers such as IBM, DEC, SUN, and MASSCOMP.

In FY86 we became a field test site for C, a programming language developed by AT&T that is a superset of C and supports object-oriented programming. We developed an Object-Oriented Program Support class library (OOPS) and successfully

used it to implement a forms management system, thus demonstrating its practicality as an ALW programming tool. We are investigating the work being done at Carnegie-Mellon University on Project Andrew and at the Massachusetts Institute of Technology on Project Athena, two large workstation efforts funded by IBM and DEC with goals similar to ours. Next fiscal year we plan to extend the OOPS library with facilities for implementing direct manipulation graphical user interfaces and perhaps data acquisition. A SUN-3 and an IBM PC-RT have been ordered, and will be used to evaluate software obtained from the Andrew and Athena projects.

NIH Campus Area Network

W.L. RISSO
with: R. Fico, T. Kuhfuss (DCRT/CSL).

Starting in 1985, CSL began developing a campus-wide electronic network which will encourage the sharing and dissemination of computer data such as molecular graphics and video images from biomedical and clinical research, and will provide a mechanism for interconnection of scientific and engineering computer workstations and local area networks.

Several explicit data communications requirements were developed during this past year, including a computer graphics network, transmission of electron microscopy and NMR data, and interconnection of several local networks. A concept design of a campus wide network has been completed, specifying a broadband cable plant installed in the now vacant pneumatic tube system (where it exists) and in other underground conduits elsewhere. The design also specifies fiber optic cable in the conduits, anticipating some immediate need, but more importantly providing a migration path from the broadband as technology changes. We successfully completed a broadband link between two NIH buildings for use in testing several networking applications. Work on engineering specifications for the complete design has begun.

We plan to provide a network channel to interconnect the many scientific minicomputer users represented by the NMR and the image processing group; a very high-speed Apollo network to service the molecular graphics groups; a campus-wide Ethernet to interconnect Office Area Networks; and a variety of video channels for medical images and closed circuit television. During the next year we plan to install cable to interconnect buildings 12, 13, 10, and 29, and to extend the cable to other buildings in early 1988.

Expert Systems in Medicine

D. SYED
with: K.M. Kempner, H. Fredrickson, J.J. Knight (DCRT/CSL); J.E. Parrillo, M.D., M.A. Mazer, M.D., G.L. Akin (CC/CCM).

This project involves the development of expert systems in the medical environment. Expert systems represent feasible applications of artificial intelligence techniques. They are knowledge-based, in that they contain knowledge contributed by experts, and organized, by knowledge engineers. Generally, they function best in specific, narrowly defined, yet still complex, problem areas. A very important characteristic of these systems is that decisions and recommendations are explained and justified to the user. An initial objective for the project is to develop, in collaboration with the Critical Care Medicine Department of the Clinical Center, a Therapy Advisor Expert System for use in an Intensive Care Unit. The drug administration protocol includes the capability for long-term dose maintenance and eventual dose tapering.

Personal computer-based technology (IBM PC-XT or PC-AT) has been utilized in conjunction with commercial expert system shells and an original generated BASIC approach.

A knowledge base consisting of approximately 800 rules was developed as part of the Therapy Advisor Expert System. These rules were implemented on a PC-AT using a generated BASIC approach. Implementation of a revised generalization of the rule base is currently underway. A survey of artificial intelligence languages and shell programs continued and two small Expert Systems were developed to provide specific shock diagnosis and to diagnose wide complex tachycardias using a shell system.

The successful implementation of expert systems technology in dynamic medical problem areas can be expected to pave the way for the design of more sophisticated research protocols. Expert systems will effectively allow the researcher to be continually present during the execution of protocols of long duration, and to modify, within protocol limits, the necessary medical interventions in realtime.

Clinical testing of the prototype system will begin upon completion of the generalized rules. Rules for blood gas and respiratory protocols must be added. Diagnosis-specific rule sets must also be appended. Design of sophisticated trend functions, online system implementation, integration of deep knowledge from drug models and knowledge base refinement through performance assessment, constitute the major future goals.

Job Tracking and Control System for the Medical Arts and Photography Branch

L.W. FREEMAN 6 *with:* H.A. Fredrickson (DCRT/CSL); P.A. Lewis, R.B. Winterrowd (DRS/MAPB).

Besieged by an ever increasing volume of files, forms, and a need for information retrieval, the DRS Medical Arts and Photography Branch enlisted CSL to develop a job tracking and control system. In addition to the need for a staged implementation of job tracking, other prominent requirements include: high reliability, expandibility, archiving capability, and ultimately a local billing capability. During late FY85, CSL analyzed the operational requirements and designed a system involving a network of IBM personal computers.

The current configuration consists of 5 PC's for the Graphics Section, 3 PC's for the Design Section, and 3 PC's for the Administrative Office. These 11 PC's are linked with 2 3Com 3-Servers in the 3Com 3Plus Local Area Network. The Data Base Management System (DBMS) currently under evaluation is dBASE III Plus, which seems to be adequate for Graphics and Design. There is some question as to whether dBASE will be fast enough to handle the larger volume of work that photography processes.

Implementation of the first phase, which includes job tracking and control, remote billing, archiving, and flexible information reporting and retrieval for the Graphics and Design Sections, is almost complete. In addition, a system for calculating the annual budget for the Graphics Section is about 75 percent complete. This budget system will be easily adapted to the other sections and the Administrative Office.

Future work involves selection of a method (dBASE III Plus, Clipper, DBIII Compiler, C, BASIC) for implementing the Photography Section system and proceeding with the implementation. With some exceptions, this effort will be very similar to that required for the other sections and much of the software already written for the other sections will be easily adaptable to Photography's needs.

Nuclear Medicine Computer System

H. OSTROW
with: S. Bacharach (CC/NM), D. Carpenter (DCRT/CSL); S. Larson, M.D., M. Green, M. Feldman (CC/NM).

CSL has continued its support of the Nuclear Medicine Department by assessing their changing and expanding processing needs and translating these into computer requirements that are anticipated to grow 10- to 30-fold over the next few years. This year Nuclear Medicine installed two multislice Positron emission tomography (PET) systems for a total of three, and added a third single photon emission computed tomography (SPECT) system. Nuclear Medicine now has brought online two in-house cyclotrons for generating various isotopes for PET systems.

Last year a Request for Proposals (RFP) for a department-wide computer system was released. This year a contract was negotiated and signed to provide data processing capabilities for both the routine clinical activities and a multitude of research projects. The initial system was installed, which consisted of data acquisition systems (DAS's) that are connected via a network to a large host system. The DAS's will be used for acquisition and processing of routine clinical studies and the host will eventually be used for central storage and display and will provide the computer processing capabilities needed for the research activities.

We are working closely with Nuclear Medicine to develop an integrated system that will easily allow central storage of all the multimodality images, along with retrieval and display of the data and images from any location in the department. In addition to sharing system responsibility, our particular involvement is in the development of additional network capabilities both for digital and video transmission in a multivendor environment and for data base management capabilities.

Neuromagnetometer Computer System

R.L. MARTINO, Ph.D., L.D. NADEL, Ph.D.,
with: J.E. Sullivan (DCRT/CSL); S. Sato, M.D., D.F. Rose, M.D., R.J. Porter, M.D., (NINCDS/MNB); P.D. Smith, Ph.D., J.L. White, W.S. Friauf (DRS/BEIB).

The Medical Neurology Branch, NINCDS, the Biomedical Engineering and Instrumentation Branch, DRS, and the Computer Systems Laboratory, DCRT are collaborating on a research project to localize noninvasively epileptic discharge sources within the human brain by using neuromagnetic recording in conjunction with conventional electroencephalogram (EEG) recording.

Many patients with seizure disorders exhibit low-level cellular discharges between seizures, indicated by interictal spikes in their EEG and magnetoencephalogram (MEG) recordings. This project involves the development of computer techniques for automating and enhancing the procedure that is presently used by NINCDS neurologists to determine the intracranial locations of the sources of interictal spikes in patients with epilepsy.

The required MEG and EEG signals are acquired with a system purchased from Biomagnetic Technologies, Inc. (BTi) and placed in operation during FY86. It includes a seven-channel SQUID (superconducting quantum interference device) for measuring the MEG signal from seven sites on the head simultaneously, a combined BTi and Hewlett-Packard (HP) data acquisition system for acquiring the EEG and MEG signals, and an HP 9000 computer workstation for signal processing and graphical display functions.

CSL designed and built a 32-channel signal selection and conditioning interface that was added to the data acquisition system. This interface provides the capability to select which signals go to the analog-to-digital converter inputs, amplify and add an offset voltage to the signals, and hold the value of the signals for the same instant of time using sample and hold amplifiers. A high-resolution graphics terminal was added to the HP workstation to provide the relevant display of results to the medical staff. The capability to transfer data files between the HP computer system and IBM personal computers (PC's) was implemented so that the IBM PC's could be used as remote waveform analysis and display tools.

In the future, the project will focus on the automation of the detection of interictal spikes from the EEG and MEG signals and the extraction of relevant features characterizing the detected waveforms. The information obtained from these features will be used with values extracted from the raw waveforms to generate the graphical displays needed to determine the epileptic foci.

DCRT Local Area Network (LAN)

W.L. RISSO
with: T. Kuhfuss, R. Fico (DCRT/CSL).

In order to develop expertise in LAN technology, and to provide LAN interconnection of some 70 IBM compatible personal computers as well as numerous terminals, modems, and computer systems, CSL has installed an extensive Ethernet serving DCRT. We selected the Ethernet LAN because it is an established standard, supported by products from a broad spectrum of companies. The network was designed and installed in FY84, and extended to Building 12B in FY85.

This year the DCRT LAN was extended to Building 13 via a broadband link, and connected to a separate Ethernet there. Within Buildings 12/12A some 25 additional nodes were added to the network, which now spans 1,250 meters and interconnects 70 IBM PC's and eight host computers. Eight 2400 baud modems were added, providing shared dial in/out access for DCRT network users.

In collaboration with the DCRT Personal Workstation Office, we expect to upgrade the network software to allow internetworking of the Building 12/12A Ethernet with an Ethernet in Building 31 serving DCRT offices there. This link will be via telephone lines, anticipating the installation of a campus broadband network. We also expect to install an intelligent network monitor to provide dynamic network status and a statistical history of network activity.

Audiology ABR Analysis and Interpretation Expert System

J.M. DELEO
with: A. Pikus, A.M. Grimes (CC/OD).

A series of responses is produced by the nervous system during the 500 millisecond interval following the presentation of click or tone stimulus to the ear. Responses occuring in the first 10 milliseconds post-stimulus are referred to collectively as the Auditory Brainstem Response (ABR), since they arise from brainstem structures. The ABR is used to assess the functional integrity of these structures, particularly the pons. Deviation from the expected, normative ABR template could provide supportive evidence in diagnostic evaluation.

Our objective in this new project is to build an expert system to analyze and interpret ABR signals produced by patients examined in the NIH Clinical Center Audiology Department. This involves acquisition of the knowledge base needed to model the cognitive processes invoked in the tasks of significant peak determination and diagnostic interpretation. To date, an adequate knowledge base for peak determination in normal and near-normal ABR's has been elicited and a robust peak detection algorithm has been written. Development of the diagnostic inferencing knowledge base was started but has been temporarily suspended due to the departure of an audiologist. A survey of appropriate equipment in which to install the developed expert system software has been ongoing.

PC's in the Laboratories

J.S. DEL PRIORE
with: J.E. Sullivan, R.L. Tate, Ph.D. (DCRT/CSL).

Traditionally, CSL has collaborated with, or provided support to, investigators whose research required the use of computers in laboratory or clinical situations. In anticipation of widespread use of personal computers in NIH laboratories, this project was initiated to support laboratory applications of PC's.

In FY86, this support project has included advice on system configurations, suitable laboratory software packages, hardware interfacing equipment, data acquisition techniques, and when appropriate, has suggested alternative, more suitable approaches to a problem. In addition, a course on using PC's for laboratory data acquisition was offered. It covered signal and instrument investigation, analog and digital signals, data collection and storage, and data analysis and display.

Anticipated future activity will continue to include consulting. The course will be offered semi-annually. As more laboratories acquire PC's for data acquisition and analysis, scientists' needs are expected to shift from advice on system configurations and data collection approaches to assistance with actual data acquisition situations. Some of these activities may result in full laboratory data acquisition or automation projects requiring support from other parts of CSL.

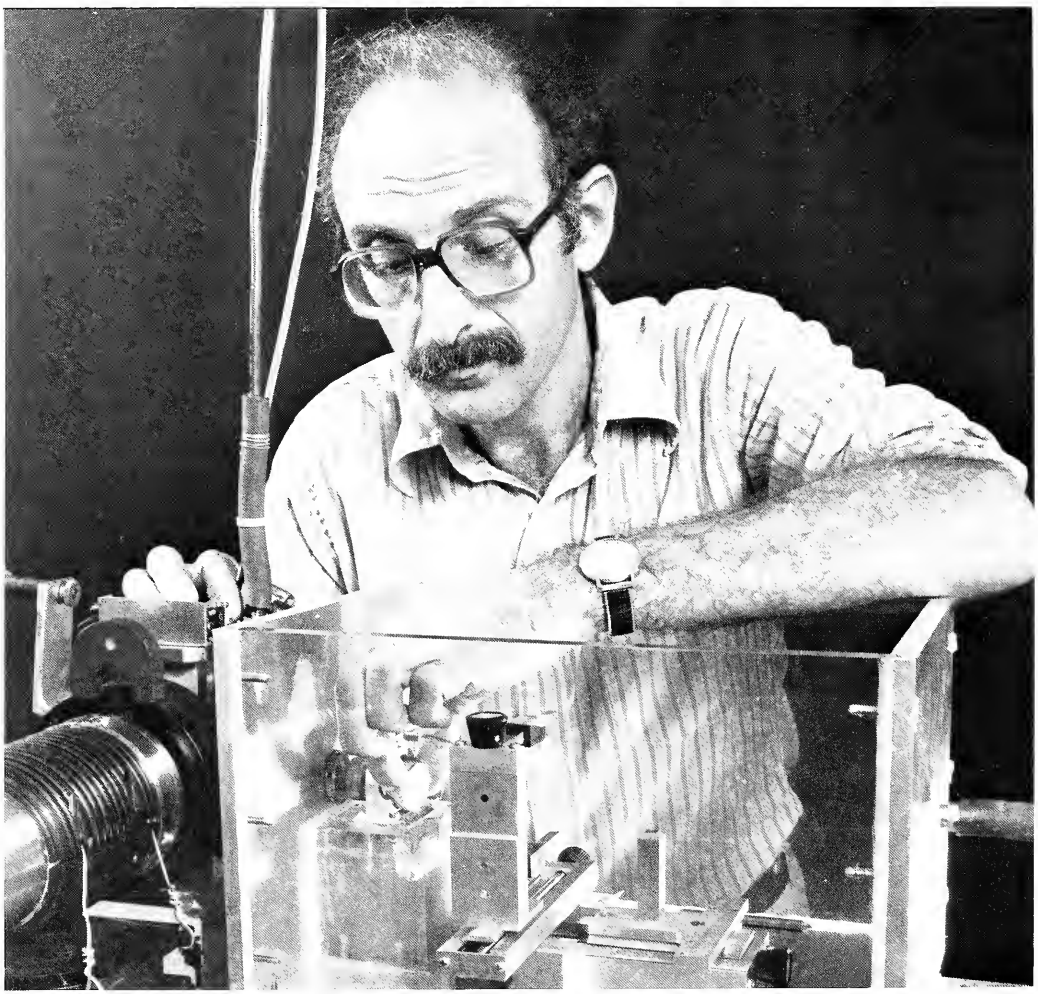
Veterinary Resources Animal Data System

H.O. OSTROW
with: P.B. Burns, T. Ingalls, C.T. Hansen, Ph.D., W. Watson, D.V.M. (DRS/VRB); P.S. Plexico (DCRT/CSL).

This project involves the development, under contract, of a Veterinary Resources Animal Data System (VRADS) for the Veterinary Resources Branch, DRS. Important goals of this system are to support research objectives in developing special strains of animals, to assist genetic monitoring so as to reduce colony loss in the event of genetic contamination, to track animal care and status, and to automate animal inventory and ordering activities. Initially the system will focus on supporting the functions of the Small Animal Section, VRB.

CSL performed a requirements analysis of VRB/SAS needs, developed a Request for Proposals for a computer-based animal data management system, and assisted DRS in evaluating and negotiating a contract. The contract was awarded in the fourth quarter of FY83. Since then, CSL has served as a resource to the DRS Project Officer, providing management and technical consulting as needed. This role has become increasingly important during FY86 as more and more problems with contractor performance have come to light. During this period CSL has assisted the Project Officer by participating in site visits and project reviews and in determining appropriate corrective action by the contractor to increase the likelihood of a system that will satisfy VRB requirements.

V. Adrian Parsegian, Ph.D. places DNA sample in the path of an x-ray beam. This work is part of a project for the direct measurement of physical forces between macromolecules.



Physical Sciences Laboratory

George H. Weiss, Ph.D., Chief

The Physical Sciences Laboratory (PSL) uses chemistry, physics, applied mathematics and biophysics to research problems that arise in a biomedical setting. Part of the work consists of internally generated research projects, and the remainder consists of collaborative research within NIH as well as with investigators at universities throughout the world.

The Laboratory consists of four members on the doctoral level, one at the masters level, a fluctuating number of visitors, as well as supporting staff. A sampling of current research indicates the wide variety of questions tackled by members of the PSL. Some of these include: the measurement and interpretation of forces that operate on a molecular level in biological structures; the application of small angle neutron scattering to probe interactions between macromolecules in concentrated protein solutions; development of relevant theory to measure the depth of penetration of laser beams into skin; the development of a theory of optimal preprocessing of NMR data for the estimation of parameters; and the design of computer graphical systems for use by biochemists. Thus, the work consists of a mixture of theory and experiment with the theory never straying far from the experimental milieu.

Many collaborations exist between members of the PSL and investigators at NIH and at other institutions of higher learning. Examples of the first consist of a joint project with BEIB on the medical use of laser Doppler techniques; a collaborative effort with investigators in NHLBI on the optimal design of NMR experiments; a joint effort with members of NIADDK on the structural transitions occurring in lipid-water suspensions; and the development, together with other members of DCRT, of a molecular graphics system for use by chemists. Examples of collaborative research outside of NIH include a joint study of mathematical methods for the interpretation of crystallographic data together with crystallographers in England and Israel; the development of instrumentation for measurement of electrical properties of whole cells together with a researcher in Paris; and a joint project on reaction rate theory with several researchers in Israel.

Applications for Medicine, Science

Laser light scattering has found many applications in medicine. Drs. Nossal, Weiss, and Havlin of PSL have developed a theory allowing one to measure properties of the penetration depth of laser photons in skin. The theory has been verified in many experiments performed by Dr. R. Bonner in BEIB. Such a theory is needed to facilitate the use of lasers for both diagnostic and therapeutic purposes, because it allows one to monitor the effects of the laser beam from external measurements.

Many experimenters have studied the interaction of macromolecules in dilute solution, because the interpretation of data from such experiments is relatively straightforward. Dr. Nossal, in collaboration with researchers at the National Bureau of Standards, has initiated experiments that use small angle neutron scattering to measure interaction effects for macromolecules in concentrated solutions. A theory was developed to translate data into chemically relevant parameters, and samples of bovine serum albumin were probed using this technique to determine the applicability of the theory with excellent results.

Dr. Zimmerberg, together with collaborators both in this country and abroad, has developed instrumentation to make simultaneous measurements of physiological and anatomic properties of living cells, while controlling the internal milieu. Preliminary experiments have been carried out using this instrumentation on mast cells, which show large capacitance changes at the instant of secretion.

Dr. Weiss, together with Dr. Ferretti of NHLBI and Dr. Byrd of the Center for Drugs and Biologics, has developed a theory of accuracy and precision in the measurement of NMR parameters when apodization is used. The theory will allow the experimenter to choose the most useful apodization function in maximizing the obtainable precision of such measurements. These measurements are of critical importance in the interpretation of two-dimensional Fourier Transform experiments.

Dr. Parsegian was an invited speaker at a number of meetings on aspects of biophysical research. These include a meeting on anhydrous biology in Bellagio, Italy; a conference on the biophysics of cell surfaces in Heringsdorf, E. Germany; the Faraday Discussions on lipid assembly in Loughboro, England; and the Biorheology Congress in Vancouver. Dr. Weiss has given invited talks at the International Union for Pure and Applied Physics meeting on statistical mechanics in Boston, and the American Statistical Association meeting in Chicago. Dr. Parsegian has been appointed to the editorial board of Biorheology and Dr. Weiss has been appointed to the editorial board of Chemometrics and Intelligent Laboratory Systems.

Longer-term Research

All of the research mentioned so far represents the beginnings of longer-term projects. The projects involving instrumentation have so far focused on development of techniques and overcoming design problems. All of these projects represent a first phase. The second phase involves implementation of the systems with application to biological systems, which are significant in a medical context. As an example, small angle neutron scattering has been used to detect protein aggregates in deoxygenated sickle red blood cells. Further studies of this system will be carried out using facilities at the National Bureau of Standards.

Several fruitful collaborations have been developed in the application of dynamic light scattering techniques to chemical systems between Dr. Nossal and other scientists at NIH. Together with Dr. Gershfeld of NIADDK these optical methods will be used to measure further examples of structural transition that occur in lipid-water suspensions. They will also be used in a joint investigation with Drs. Ehrenstein and Russel of NINCDS on the release of peptides from neurosecretory vesicles.

We foresee further work on the interaction between apodization and precision in the estimation of parameters derived from NMR measurements.

Publications

Barouch, E., Matijevic, E., and Parsegian, V. A.: On the Accuracy of the Derjaguin Approximation for the Electrostatic Double Layer Interaction between Curved Surfaces Bearing Constant Potentials. *J. Chem. Soc.*, Faraday Trans. II (in press).

Bezanilla, F., Parsegian, V. A., and Zimmergerg, J.: The response of squid giant axon potassium channels to osmotic stress. *Biophys. J.* 49: 161a, 1986.

Bonner, R. F., Nossal, R., Havlin, S., and Weiss, G. H.: A model for photon diffusion in turbid biological media. *J. Opt. Soc. Amer. A.* (in press.

Bunde, A., Havlin, S., Nossal, R., and Stanley, H. E.: Anomalous trapping: effect of interaction between diffusing particles. *Phys. Rev.* B32: 3367-3370, 1985.

Bunde, A., Havlin, S., Nossal, R., Stanley, H. E., and Weiss, G. H.: On controlled diffusion-limited drug release from a leaky matrix. *J. Chem. Phys.* 83:5909-5913, 1985.

Evans, E. A., and Parsegian, V.: The action of thermal fluctuations on forces within lamellar arrays. *PNAS* (in press).

Finkelstein, A., Zimmerberg, J., and Cohen, F. S.: Osmotic swelling of vesicles: its role in the fusion of vesicles with planar phospholipid bilayer membranes and its possible role in exocytosis. *Ann. Rev. Physiol.* 163-174, 1986.

Gaylord, R. J., diMarzio, E. A., Lee, A., and Weiss, G. H.: The relaxation of an unattached chain in a cross-linked network: A span analysis of reptation. *Polymer Comm.* 26: 337-338, 1985.

Gaylord, R. J., Weiss, G. H., and diMarzio, E. A.: A continuous random walk model of the viscoelastic behavior of cross-linked polymers. *Advances in Elastomers and Rubber Elasticity* (in press).

Gaylord, R. J., Weiss, G. H., and diMarzio, E. A.: Nonequilibrium mechanical response of a cross-linked network. *Amer. Chem. Soc.*, pp. 927, 1986; *Macromolecules* (in press).

Gershfeld, N. L., and Nossal, R. J.: Studies of phospholipid bilayer assembly in water. *A. C. S. Polymer Preprints* (in press).

Gershfeld, N. L., Stevens, Jr., W. F., and Nossal, R. J.: Equilibrium studies of phospholipid bilayer assembly. Faraday Discuss. Chem. Soc. (in press).

Harris, A. L., Walter, A., and Zimmerberg, J.: Vesicles containing functional voltage-dependent anion channels (VDAC) can be purified by a transport-specific density shift. *Biophys. J.* 49: 521a, 1986.

Havlin, S., Kiefer, J. E., Weiss, G. H., Ben-Avraham, D., and Glazer, Y.: Properties of the skeleton of aggregates grown on a Cayley tree. *J. Stat. Phys.* (in press).

Havlin, S., Movshovitz, D., Trus, B., and Weiss, G. H.: Probability densities for the displacement of random walks on percolation clusters. *J. Phys.* 18A: L719-L722, 1985.

Havlin, S., Nossal, R., and Trus, B.: Cluster growth model for tree-like structures. *Phys. Rev.* A32: 3829-3833, 1985.

Havlin, S., Nossal, R., Trus, B., and Weiss, G. H.: Diffusion on tree-like clusters. *Phys. Rev.* B31: 7497-7499, 1985.

Havlin, S., Trus, B., and Weiss, G. H.: A diffusion model for transport on loopless aggregates. *J. Phys. A: Math. Gen.* 18: L1043-L1048, 1985.

Havlin, S., Trus, B. L., and Weiss, G. H.: A phase transition in the dynamics of an exact model for hopping transport. *Phys. Rev. Lett.* (in press).

Lee, B.: A procedure for calculating thermodynamic functions of a cavity formation from the pure solvent simulation data. *J. Chem. Phys.* 83: 2421-2425, 1985.

Lipman, D. J., Pastor, R. W., and Lee, B.: Local sequence patterns of hydrophobicity and solvent accessibility in soluble globular proteins *Biopolymers* (in press).

Liu, J., and Zimmerberg, J.: Calcium-stimulated secretion in sea urchin eggs: exocytosis proceeds in vitro in the absence of other ions. *Biological Bulletin* 169: 562, 1986.

Nossal, R.: An analysis of the elasticity of cytoskeletal networks. *A.C.S. Polymer Preprints*. 27: 241-242, 1986.

Nossal, R., Glinka, C. A., and Chen, S. H.: SANS studies of concentrated protein solutions. I. Bovine serum albumin. *Biopolymers* 25: 1157-1175, 1986.

Parsegian, V. A., Crawford, N., McNeel, M., Douglas, M., and Horton, M.: Electronic submission of scientific manuscripts. *Cancer Investigation* (in press).

Parsegian, V. A., Rand, R. P., Fuller, N. L., and Rau, D. C.: Osmotic stress for the direct measurement of intermolecular forces. In Packer, L. (Ed.): *Methods in Enzymology; Biomembranes: Protons and Water: Structure and Translocation*. New York, Academic Press (in press).

Parsegian, V. A., Rand, R. P., and Rau, D. C.: Lessons from the direct measurement of forces between biomolecules. In Safran, S. (Ed.): *Physics of Complex and Supermolecular Fluids*. John Wiley & Sons (in press).

Parsegian, V. A., Rau, D. C., Evans, E. A., and Rand, R. P.: Unexpected features of forces measured between membranes or macromolecules. *Studia Biophysica*. 110: 71-76, 1985.

Parsegian, V. A., Rau, D. C., and Zimmerberg, J.: Structural transitions induced by osmotic stress in anhydrous biological systems. In Leopold, C. (Ed.): *Membranes, Metabolism and Dry Organisms*. Cornell University Press, Ithaca, NY (in press).

Politowicz, P. A., Kozak, J. J., and Weiss, G. H.: Random walks on finite high-dimensional cubic lattices with a single trap. *Chem. Phys. Lett.* 120: 388-392, 1985.

Shmueli, U., and Weiss, G. H.: Centric, bicentric, and partially bicentric intensity statistics. In Wilson, A. J. C. (Ed.): *Structure and Statistics in Crystallography*. Guilderland, NY, Adenine Press, 1985, pp. 53-66.

Shmueli, U., and Weiss, G. H.: Exact joint distribution of E(h), E(k), and E(hk) and the probability for the positive sign of the triple product in the space group P1. *Acta Crystallogr.* (in press).

Shmueli, U., and Weiss, G. H.: Exact joint probability distribution for centrosymmetric structure factors. Derivation and application to the sigma1 relation in the space group P1. *Acta Crystall.* A41: 401-408, 1985.

Shmueli, U., and Weiss, G. H.: Exact random-walk models in crystallographic statistics. III. Distributions of E for space groups of low symmetry. *Acta Crystallogr.* (in press).

Weiss, G. H.: Competitive trapping effects in a set of partially absorbing traps. *J. Stat. Phys.* (in press).

Weiss, G. H.: On a generalized transport equation for chromatographic systems. *Proc. of the meeting on Transport in Random Media* (in press).

Weiss, G. H.: Overview of theoretical models for reaction rates. *J. Stat. Phys.* 42: 3-36, 1986.

Weiss, G. H.: Passage times. *Encyc. Stat. Sci.* 6: 630-635, 1985.

Weiss, G. H.: Random walks. *Encyc. Stat. Sci.* (in press).

Weiss, G. H.: Saddle-point approximations. *Encyc. Stat. Sci.* (in press).

Weiss, G. H.: Statistics in crystallography. *Encyc. Stat. Sci.* (in press).

Weiss, G. H.: Tauberian theorems. *Encyc. Stat. Sci.* (in press).

Weiss, G. H.: Walds identity. *Encyc. Stat. Sci.* (in press).

Weiss, G. H., Bendler, J. T., and Dishon, M.: Analysis of dielectric loss data using the Williams-Watts function. *J. Chem. Phys.* 83: 1424-1427, 1985.

Weiss, G. H., diMarzio, E. A., and Gaylord, R. J.: First passage time densities for random walk spans. *J. Stat. Phys.* 42: 567-572, 1986.

Weiss, G. H., and Havlin, S.: Non-Markovian reaction sites and trapping. *J. Chem. Phys.* 83: 5670-5672, 1985.

Weiss, G. H., and Havlin, S.: Some properties of a random walk on a comb structure. *Physica* 134A: 474-482, 1986.

Weiss, G. H., Havlin, S., and Bunde, A.: On the survival probability of a random walk on a finite lattice with a single trap. *J. Stat. Phys.* 40: 191-199, 1985.

Weiss, G. H., Salazar, A. M., Vanee, S. C., Grafman, J. H., and Jabbari, B.: Predicting posttraumatic epilepsy in penetrating head injury. *Arch. of Neur.* (in press).

Weiss, G. H., and Shmueli, U.: Fourier representations of pdf's arising in crystallography. *J. Res. NBS.* 90: 507-513, 1985.

Whitaker, M., and Zimmerberg, J.: High colloid osmotic pressures inhibit dispersal, the second stage of exocytosis in sea urchin eggs. *Biological Bulletin* 169: 564, 1985.

Whitaker, M., and Zimmerberg, J.: Inhibition of exocytosis in sea urchin eggs by polymer solutions. *J. Physiol.* (in press).

Zimmerberg, J., and Parsegian, V. A.: Changes in polymer-inaccessible space as a measure of volume change during opening and closing of voltage-dependent ionic channels: the voltage dependent anion channel (VDAC). *Nature* (in press).

Zimmerberg, J., and Parsegian, V. A.: Polymer-inaccessible space as a measure of the volume change during channel opening and closing: VDAC channels. *Biophys. J.* 45: 59a, 1984.

Zimmerberg, J., Sardet, C., and Epel, D.: Exocytosis of sea urchin egg cortical vesicles in vitro is retarded by hyperosmotic sucrose: kinetics of fusion monitored by quantitative light-scattering microscopy. *J. Cell Biol.* 101: 2398-2410, 1985.

Zimmerberg, J., and Whitaker, M.: Capacitance measurements confirm hyperosmotic inhibition of fusion in sea urchin eggs. *Biophys. J.* 47: 172, 1985.

Zimmerberg, J., and Whitaker, M.: Elevated colloid osmotic pressure reversibly inhibits calcium-dependent exocytosis in sea urchin eggs. *J. of Physiol.* 253: 85, 1985.

Zimmerberg, J., and Whitaker, M.: Irreversible swelling of secretory granules during exocytosis caused by calcium. *Nature* 315: 581-584, 1985.

Research Projects

Molecular Forces in Cellular Assembly

V. ADRIAN PARSEGIAN, Ph.D.
with: E. Barouch, Ph.D. (Clarkson Univ., NY); E. A. Evans, Ph.D. (U. British Columbia, Canada); S. Gruner, Ph.D. (Princeton Univ., NJ); A. L. Harris, Ph.D. (DCRT/PSL, J. Hopkins Univ.); R. P. Rand, Ph.D. (Brock Univ., Canada); D. Rau, Ph.D. (NIADDK); J. Zimmerberg, Ph.D. (DCRT/PSL).

One usually thinks of cell membrane lipids in the form of the lamellar sheets in which they are orginally found. It appears from our recent work that the addition of relatively small amounts of non-polar hydrocarbons can create non-lamellar arrangements similar to those that occur during such membrane fusion processes as cellular secretion. We have determined the chemical potential of phospholipids in the inverted hexagonal structure finding that the lipid hydrocarbon chains pack to fill space with negligible strain. Measuring the work of bending lipid layers we have found that their bending elasticity modulus is essentially the same for planar

structures as for layers with small spontaneous radii of curvature.

In these lipid systems we find that the work of bringing bodies together is the hydration force of removing structured water solvent from their surfaces. We have been able to modify forces between DNA macromolecules by altering the entropy of water in the bathing solution. To do this we have used different anionic solutes-- chaotropic perchlorate, chloride, and order-forming sulphate--to change the entropy of the bathing medium. We have found that relatively small changes in the ionic composition of the bathing solution change the properties of water solvent enough to control molecular assembly. These experimental findings are tightly coupled to theoretical analyses to formulate and to compute interactions. We have evaluated the accuracy of the well-known Derjagin approximation for converting the interaction between curved surfaces into that between planar surfaces of the same material.

Consulting Services

GEORGE H. WEISS, Ph.D.
with: J. E. Kiefer (DCRT/PSL); R. A. Brooks, Ph.D. (NINCDS).

We have developed a theory that allows one to estimate measures of precision for rate constants found from PET scan measurements. The theory also allows one to design optimal experiments for such estimates.

Instrumental Analysis

GEORGE H. WEISS, Ph.D.
with: V. Bloomfield, Ph.D. (Univ. of Minnesota); A. Byrd, Ph.D. (NIDR); M. Dishon, Ph.D. (Weizmann Institute); J. A. Ferretti, Ph.D. (NHLBI); J. E. Kiefer (DCRT/PSL); U. Shmueli, Ph.D. (Tel-Aviv Univ., Israel).

This project includes a number of different investigations. We have initiated a project together with Dr. Ferretti (NHLBI) on the choice of optimal apodization functions for the measurement of areas and volumes in Fourier transform NMR. Apodization functions are used to preprocess data before analyzing their physical content. We have found that Gaussian apodization functions leads to a considerable increase in the precision of area measurements under curves generated in one-dimensional NMR. This agrees with earlier observations for which no theory has been available. Together with Dr. Ferretti we have completed an invited review article on optimal methods for the measurement of spin-lattice relaxation times in NMR.

In a joint project with Professor Shmueli of Tel-Aviv University we have further developed the theory of exact representations of probability densities that are used in crystallography. We have calculated a number of such densities useful in the application of intensity statistics, and are presently working on representations of the densities of phase invariants used in direct methods of phase determination. Progress on this problem is slow because of the complicated calculations that are required.

We have, together with Professor Bloomfield, a visiting FIC Fellow, initiated a study of the effects of pore size distribution relative to the size of macromolecules in gel electrophoresis. This study is aimed at the determination of qualitative effects in gel electrophoresis, and involves a combination of simulation and exact methods of solution.

Studies in Mathematics and Statistics

GEORGE H. WEISS, Ph.D.
with: E. A. diMarzio, Ph.D. (National Bureau of Standards); R. J. Gaylord, Ph.D. (Univ. of Illinois); S. Havlin, Ph.D. (Bar-Ilan Univ., Israel); J. E. Kiefer (DCRT/PSL); A. Szabo, Ph.D. (NIADDK).

We have continued work on projects related to the theory of reaction rates for chemical reactions. Present projects include the study of statistical properties of the displacement of diffusing particles in a field of static traps, and the theory of survival times of particles in a field of static traps subjected to time-varying forces. A second project relates to the microscopic kinetics of entangled polymers. Together with Dr. Szabo we are writing a review of first passage time problems in chemical physics.

Studies on the Effect of Solvent Around Biological Macromolecules

B. LEE, Ph.D.
with: D. Lipman, Ph.D. (NIADDK); R. Pastor, Ph.D. (FDA).

Ever since Dr. C. Anfinsen's pioneering work, it has been the fondest hope of many protein physical chemists to be able to predict the three-dimensional structure of a globular protein from its amino acid sequence. One of the major properties of the amino acids that are used towards this goal is their hydrophobicity. However, the extent to which the hydrophobicity properties of amino acid residues can aid in predicting the structure has not been quantitatively measured. In the past year, Dr. D. Lipman of the Arthritis Institute, Dr. R. Pastor of the FDA and I made a general study of the relationship between the hydrophobicity pattern and an important structural property--the accessibility of individual amino acid residues. Using crystal structures and the native and randomly shuffled sequence data sets, we found that we could indeed quantitatively measure the power of the hydrophobicity pattern in predicting the accessibility pattern of globular proteins. We have found, unfortunately, that there is a severe limitation in the amount of structural information one can extract from the hydrophobicity pattern represented by the native sequence data, implying that even rudimentary structure prediction must include considerations other than hydrophobicity alone.

Development of Apollo Computer System for Modeling Macromolecules

B. LEE, Ph.D.
with: B. Brooks, Ph.D., R. Feldmann, Ph.D. (DCRT/OD); R. Pastor, Ph.D. (FDA).

A large part of the past year was spent learning the UNIX operating system, the C language, and the Silicon Graphics IRIS workstation. I have now developed a molecular graphics system on the IRIS in C. The system is particularly suited for a realtime manipulation of macromolecules. It is menu-driven so that even an occasional novice user can start using the system without prior preparation. By September 1986, we hope to link this graphics package with the energy minimization--molecular dynamics program that Dr. B. Brooks is developing on the STAR100. Once this linkage is completed, we will have one of the world's most powerful tools for modeling biological macromolecules.

Biophysical Analysis

RALPH J. NOSSAL, Ph. D.
with: J. Hofrichter, Ph.D. (NIADDK/LCP); G. H. Weiss, Ph.D. (DCRT/PSL); B. Trus, Ph.D. (DCRT/CSL); S. Havlin, Ph.D. (Bar-Ilan Univ., Israel); S. H. Chen, Ph.D. (Dept Nucl. Engr., MIT); C. Glinka, Ph.D. (Reactor Div., NBS); A. Bunde, Ph.D., H. E. Stanley, Ph.D. (Physics Dept., Boston University).

We have further developed a scheme utilizing small angle neutron scattering (SANS) to probe interactions between macromolecules in highly concentrated protein solutions. Using this technique we have systematically studied properties of bovine serum albumin (BSA) samples to test the theoretical analysis that is used to extract molecular size and charge from experimental data. Studies also were performed on hemoglobin (Hb) solutions, the results of which were employed to devise techniques for examining protein interactions within intact erythrocytes and other biological vesicles. The contrast match point for vesicle membranes has been determined and detection of protein aggregates in deoxygenated sickle red blood cells was demonstrated. Several investigations based on this methodology now are in progress.

We have undertaken investigations into the properties of polymer networks and related amorphous structures. For this purpose we have developed mathematical models to describe the formation of cytoskeletal networks. These allowed us to investigate complex relationships between nucleation. Polymerization, crosslinking, chain termination and chain scission procedures were developed for obtaining elasticity contours (e.g., dependences of shear modulus on Ca concentration), which are needed for theories of cell movement. Quantitative gelation assays for assessing the activity or cytoskeletal binding proteins also were analyzed.

Correlation Function Spectroscopy/Laser Light Scattering

RALPH J. NOSSAL, Ph.D.
with: R. Bonner, Ph.D. (DRS/BEIB); G. Ehrenstein, Ph.D. (NINCDS/LB); N. Gershfeld Ph.D., (NIADDK/LBP); S. Havlin, Ph.D. (Bar-Ilan Univ., Israel); J. Russell, Ph.D. (NICHHD/LNN); G. W. Weiss, Ph.D. (DCRT/PSL).

In many in vivo clinical and research uses of light, incident radiation is applied to the interface between a turbid tissue and a transparent medium. Light that diffuses back to this interface and into the external transparent medium provides a noninvasive means to examine the parameters of photon diffusion within the tissue. Laser Doppler blood flow monitors, in particular, work on this principle. We have developed an analytical theory that enables calibration of such instruments from measurements of reflected light on the tissue surface. The theory relates such quantities as surface emission profile, sampling depth, and expected path length of migrating photons, to the scattering and absorption parameters of a tissue. The theoretically predicted wavelength dependence of those quantities has been verified experimentally.

Also, dynamic light scattering studies have been performed in collaboration with Dr. N. Gershfeld (NIADDK/LBP). The major emphasis of this investigation has been on the structural transitions that occur in lipid-water suspensions. The movement of polystyrene beads has been used to probe the structure of the suspensions. Transformations have been seen in bulk dimyristoylphosphatidylglycerol (DMPG) water systems at the same temperatures where discontinuities in surface pressure are discerned in film balance studies. Below the transition temperatures the dispersed lipid seems to form a jelly-like slurry, whereas above those temperatures the suspensions contain lipid vesicles. Dr. Gershfeld has performed surface film studies that indicate similar transformations may occur in the growth of biological cells. Other dynamic light scattering studies have been initiated. A particularly promising collaboration (with G. Ehrenstein and J. Russell) concerns the release of peptides from neurosecretory vesicles.

Membrane Transport

JOSHUA J. ZIMMERBERG, M.D., Ph.D.
with: F. Bezanilla, Ph.D. (UCLA, CA); A. Harris, Ph.D., V. A. Parsegian, Ph.D. (DCRT/PSL); A. Walter, Ph.D. (NCI/LTB).

To measure the change in internal volume of channels, we have been subjecting perfused preparations to positive and negative osmotic stress. The squid axon K channel volume change inferred from hypertonic stress has an upper bound of about 1,300 cubic angstroms. The mitochondrial voltage-dependent anion channel (VDAC) reconstituted into planar lipid bilayers shows a volume change of 20 to 40 thousand cubic angstroms. These numbers are large if one expects a cork or turnstile mechanism, but are quite reasonable if one imagines a rearrangement involving the entire ionic path.

The gap junction is the locus of direct transfer of ions and small molecules from cell to cell. We are attempting the incorporation of the gap junction channel into an artificial membrane system. Aliquots of the shifted vesicle fractions were added to a bilayer chamber under osmotic conditions known to promote fusion with a planar bilayer. At least three different types of channels were observed. We are presently undertaking steps to fractionate the channels further in order to isolate and identify the junctional channel, and to measure volume changes.

Membrane Fusion

JOSHUA J. ZIMMERBERG, M.D., Ph.D.
with: J. Liu, Ph.D. (Harvard College); V. A. Parsegian, Ph.D. (DCRT/PSL); R. P. Rand, Ph.D. (Brock Univ., Canada); B. Trus, Ph.D. (DCRT/CSL); M. Whitaker, Ph.D. (Univ. College London, England).

Submembrane granular fusion to cell membranes appears to be driven by granular osmotic pressure, leading to vesicular swelling and membrane merger at the contact between granular vesicle and cell membrane. We have performed experiments to learn how this swelling is accomplished. Compromising the

integrity of the granule membrane to the extent of allowing the passage of small molecules does not affect fusion. Exocytosis proceeds without ions. Polymers prevent exocytosis by preventing the disposal of the granule contents once fusion has occurred. It seems that calcium, in triggering exocytosis, triggers some alteration in the state of the internal granule phase to increase the affinity of this phase for water.

Cell Membrane Studies

JOSHUA J. ZIMMERBERG, M.D., Ph.D.
with: M. Brodwick, Ph.D. (Univ. of Texas); F. S. Cohen, Ph.D. (Rush Medical College, IL); M. Curran (Univ. of Texas); A. Marty, Ph.D. (Ecole Normale Superieure, France).

Often responses of cells studied with the tight-seal whole-cell recording technique differ from those of intact cells and change with time. We have developed an instrumental array capable of simultaneous physiologic and anatomic realtime measurements of living cells with control of the internal millieu, first using it to measure the capacitance of secretory cells. We have devised a method for purification of mast cells. Large capacitance changes are seen at the instant of secretion in mast cells, consistent with the calculated area of the secretory granule.

We also applied the cell activating compound acetylcholine to a variety of rat lacrymal gland cells to measure the liberation of intracellular calcium. We conclude that there is a loss of a diffusible factor that acts after muscarinic receptor binding and before polyphosphoinositol release. Techniques are currently being developed to prevent the loss of such factors.

Computerized Typesetting of Scientific Papers

N. CRAWFORD
with: M. McNeel, V. A. Parsegian, Ph.D. (DCRT/PSL); Science Press; Rockefeller University Press; Biophysical Society; Biophysical Discussions.

The emphasis of this year's activities has been on improved efficiency in code translation on the IBM PC-AT system. With this development, we will realize the use of personal computers as a central link between text generation on a variety of word processing systems and composition on large professional typesetting systems.

A growing feature of this transfer process is reliance on telephone transfer rather than physical transfer of magnetic disks or tapes.

Richard I. Shrager introduces PC-MATLAB, a mathematical language for personal computers.

Laboratory of Applied Studies

John E. Fletcher, Acting Chief

The Laboratory of Applied Studies (LAS) is a multidisciplinary laboratory whose staff includes physicians, mathematicians, engineers, and computer scientists. LAS operates in a task-oriented mode rather than in areas of separate disciplines. The Laboratory's approach to research problems is to examine the underlying scientific principles, to identify the appropriate mathematical and engineering concepts, and to utilize computing systems to carry out the research objectives. Many of the projects in this laboratory are collaborative efforts with bench scientists or clinical investigators at NIH or at other research centers.

The scope of our investigations ranges from direct involvement in clinical and laboratory activities, through our medical staff fellowship program, to the abstract development of mathematical methods and algorithms essential to computer modeling. The resulting software is then made available as a general research tool. These activities are carried out administratively by two sections, the **Medical Applications Section,** whose staff includes physician-scientists, electronics engineers, and computer systems analysts; and the **Applied Mathematics Section,** whose staff includes specialists in applied mathematics, computer science, and computer modeling.

Math, Data Analysis

FY86, as in FY85, saw a continued reduction in personnel and funding. As a result, LAS was forced to reduce the number of active collaborations and to limit the scope of others. In spite of these limitations progress was made in several important areas.

The applied mathematics activities were particularly active in FY85. Efforts were extended in new concepts in digital filtering, root-finding, floating-point standards, and singular value decomposition. These activities have resulted in several routines for data analysis and improvements in older methodologies. A new line search algorithm for optimization was developed and tested. Test results have been described in a manuscript that is being submitted for publication.

In FY86, the numerical methods activities were involved with the new IBM 3090 Vector Facility evaluation and testing. New and existing software for numerical solution of partial differential equations and for boundary value problems in ordinary differential equations were tested on the Vector Facility. Some other mathematical models of microcirculatory function were also tested as typical job stream cases. The gains from vectorization were found desirable, but not as dramatic as in other applications. The IBM PC mathematical software MATLAB was upgraded during the year, and is being carefully evaluated for its usefulness in various laboratory applications, including curve-fitting, data manipulation, mathematical modeling, and singular value decomposition.

Automation of a system for continuous evaluation of neurologic function in critically ill patients has been completed. Programmed stimulation and analysis now is carried out for automatically sequenced assessment of the visual, auditory, and somatosensory systems. Normal volunteers have been studied to validate system performance and to determine normal ranges.

The ECG analysis software, which was adapted for rodent ECG analysis in FY85, has been applied to rodent models of Chagas' disease. In collaboration with NIAID, a manuscript has been submitted that details the findings to date.

Using data provided by the Nuclear Medicine Department, CC, LAS analyzed a large number of parameters of radionuclide ventriculography to determine those that have the most power to classify normal, regionally abnormal, and diffusely abnormal cardiac function in a test population. A program developed by A. Albert, a former visiting LAS scientist, was used to perform logistic discriminant analysis of the data, to determine an optimal combination of parameters and the resultant classification. A paper describing these findings has been accepted for publication.

In FY86 the LAS PC activities were extended to the Local Area Network (LAN) by establishing an LAS PC-XT as a node. New software was acquired to enable file conversion among the various word processors, and enhancements were made for data analysis in data base systems. The IBM PC-AT for graphics and

imaging was installed and connected to the DCRT Ethernet (LAN). Work continues on optimizing the complimentary roles of the IBM mainframe-PC relationship for various data analysis systems.

The LAS DeAnza image processing system is being used for a wide range of image processing and algorithm development. It serves as a standard for evaluating personal computer image processing systems. Recent hardware and software developments have made an IBM PC-AT-based image processing system feasible. LAS, with the Department of Neurosurgery at Children's Hospital, has planned such a system to serve a collaborative study of spinal injury in animal models.

The NIH-wide Image Processing Group, led by LAS and CSL personnel, revised the publication *Image Processing*, which provides a directory of the wide range of image processing activities at NIH. They also brought several guest speakers to NIH to give seminars on current topics in this important field.

During FY86 LAS staff members participated in various teaching, consulting, or advisory activities. M. Horton continues to serve as an advisor to the DCRT Personal Workstation Office (PWO) and as a PWO source person for dBASE III.

M. Douglas was cited with an NIH Merit Award for her contributions to the Nuclear Medicine and other NIH image processing developments. She continues to serve as an expert consultant in this area.

R. Shrager continued to serve as consultant to NIH biochemists in areas of data analysis. He was particularly active in developing improved analyses of potentiometric data, and in exploring mathematical software for use on laboratory computers. He was a lecturer at DCRT, at Georgetown University and at the National SIAM Meeting in Boston.

J. Fletcher continued to serve as Chairman of the Mathematics and Computer Science Department of the Foundation for Advanced Education in the Sciences, and was active as a consultant on mathematical methods and software for partial differential equations. He was also an invited lecturer at various government and university sites.

J. Bailey continued as a consultant on Common Standards for Quantitative Electrocardiography, a program in medicine and public health sponsored by the European Economic Community, and also as a member of the American Heart Association Committee on Electrocardiography and Cardiac Electrophysiology. He is cochairman of the AHA Subcommittee on Computers and Electrocardiography.

New Systems, Imaging Present Challenges

Systems capable of delivering ever increasing amounts of image data are continually being added to the Nuclear Medicine Department. Therefore, the development of fast interactive algorithms for the analysis of this data is a priority task, as is the related problem of multimodality registration.

It is expected that the necessary hardware for satisfactory image processing on PC's will become available during the next year. This will lead to greatly increased use of PC's for a number of imaging applications. The development of data analysis systems, utilizing both the mainframe and the PC with the LAN as a communicating mechanism, has begun and will be carried forward during the coming year. The use of the PC with appropriate mathematical analysis software will be promoted as an alternative to older mainframe software, which is becoming obsolete. In addition, newly developed hardware and software will be acquired subject to funding constraints with the objective of making the PC a more useful data analysis tool in the laboratory environment.

The applied mathematics function will remain active in areas of laboratory computer applications, digital filtering, root-finding, mathematical modeling, and singular value decomposition. A curve-fitter has been written in the PC-MATLAB language for use in laboratory applications. Its performance will be tested in FY87.

The numerical analysis activity will consider new computing initiatives in biology that require high-speed

vector processing and will seek user friendly software for differential equation solution on laboratory PC's.

The neurologic monitoring system will be used in a canine model of septic shock in early FY87. Those parameters that are found to best correlate with pathophysiology will be used for the clinical implementation of the system in the ICU.

The MAC-16 laboratory computer system, which was acquired 15 years ago, has finally ceased to function and replacement parts for it are no longer available. Its replacement with an LSI-11-based system will be completed in this fiscal year.

The optimal minimum parameter set, which resulted from logistic discriminant analysis of the Nuclear Medicine test population, should be tested on a new larger population. Acquisition of this population is proposed over the next few years if resources permit.

Publications and Presentations

Bailey, J.J., Horton, M.R.: Can ECG criteria be standardized? In Willems, J.L., van Bemmel, J.H., Zywietz, C. (Eds.):*Computer ECG Analysis: Towards Standardization.*Amsterdam, Netherlands, North Holland Publishing Company, 1986, pp. 163-170.

Bailey, J.J., Jackson, L.K., Macfarlane, P., Vail, S.J., and Horton, M.R.: Measurement differences between 12-lead and 3-lead electrocardiographic analysis programs. *Proc. of the 13th International Congress on Electrocardiology - 27th International Symposium on Vectorcardiology* (in press).

Bieterman, M.B., and Babuska, I.: An adaptive method of lines with error control for nonlinear parabolic equations of the reaction-diffusion type. *J. of Computational Physics* 63(1):33-66, 1986.

Bunow, B., Peusner, L., Mikulecky, D.C., and Caplan, S.R.: Unifying Graphical Approaches to Dynamic Systems. *J. Chem. Phys.* (in press).

Bunow, B., Segev, I., and Fleshman, J.W.: Modeling the electrical behavior of anatomically complex neurons using a network analysis program: excitable membrane. *Biological Cybernetics*53(1):41-56, 1985.

Burgess, R.C.: Signal processing and data management considerations for continuous monitoring of evoked potentials and EEGs. Cleveland Clinic, Epilepsy Grand Rounds, Cleveland, Ohio. August, 1986.

Burgess, R.C., Le, H.V., Jacobs, E.C., Hoffman, W.D., and Bailey, J.J.: A comparative study of a posteriori wiener filtering, time varying filtering, and ARMA filtering methods using simulated evoked potentials. *MEDINFO 86, Symposium on Computer Applications in Medical Care* (in press).

Burgess, R.C., Jacobs, E.C., and Hoffman, W.D.: Design and development of a system for continuous automatic assessment of neurologic function in critically ill patients. *American EEG Society/American Epilepsy Society* (in press).

Burgess, R.C., Jacobs, E.C., and Hoffman, W.D.: A system for continuous multimodality evoked potentials. *39th ACEMB* (in press).

Burgess, R.C.: Continuous neurophysiologic monitoring of critically ill patients. Cleveland Clinic, Neurology Grand Rounds, Cleveland, Ohio. June 6, 1986.

Douglas, M.A., Albert, A., Bailey, J.J.: Logistic discriminant analysis of regional abnormalities in radionuclide ventriculography. *Computers in Cardiology* (in press).

Fletcher, J.E.: Mathematical research in partial differential equations related to facilitated diffusion and non-linear reaction diffusion systems. Air Force Institute of Technology, Dayton, Ohio, June 4, 1986.

Fletcher, J.E., and Schubert, R.W.: Axial diffusion and wall permeability effects in perfused capillary-tissue structures. *Biosystems* (in press).

Hendler, R.W., Bunow, B., and Rieske, J.: Thermodynamic and kinetic considerations of Q-cycle mechanisms. *J. of Bioenergetics and Biomembranes* 17(1):51-64, 1985.

Hendler, R.W., Reddy, K.V., Shrager, R.I., and Caughey, W.S.: Analysis of the spectra and redox properties of pure cytochrom a-a3. *Biophys. J.*49:717-729, 1986.

Jackson, L.K., Bailey, J.J., Macfarlane, P.W., Goodman, J., and Roberts, W.C.: A study of computer ECG programs in MI detection using a multidisease necropsy database. *Proc. of the 13th International Congress on Electrocardiology--27th International Symposium on Vectorcardiology* (in press).

Lehninger, A.L., Reynafarje, B., Hendler, R.W., and Shrager, R.I.: The H/O ratio of proton translocation linked to the oxidation of succinate by mitochondria. *FEBS Letters*, 192:173-178, 1985.

Lesko, L.J., Hunter, J.R., Burgess, R.C., and Rodgers, F.P.: Accumulation of nifedipine after multiple doses. *Jour. of Pharmacy and Pharmacology* (in press).

Levy, D., Savage, D.D., Garrison, R.J., Bailey, J.J., Kannel, W.B., Castelli, W.P.: Left ventricular hypertrophy: The Framingham study. In Bailey, J.J. (Ed.): *Computerized Interpretation of the Electrocardiogram X.* New York, Engineering Foundation, 1986, pp. 273-288.

Peusner, L., Mikulecky D.C., Bunow, B., Caplan, S.R.: A network thermodynamic approach to Hill and King-Altman reaction diffusion kinetics. *J. of Chemical Physics*83(11):5559-5566, 1985.

Reddy, K.V., Hendler, R.W., and Bunow, B.: Complete analysis of the cytochrome components of beef-heart mitochondria in terms of spectra and redox properties - cytochromes a-a3. *Biophysical Journal*49(3):705-715, 1986.

Segev, I., Fleshman, J.W., Miller, J.P., and Bunow, B.: Modeling the electrical behavior of anatomically complex neurons using a network analysis program: passive membrane. *Biological Cybernetics*53(1):27-40, 1985.

Setty, O.H., Shrager, R.I., Bunow, B., Reynafarje, B., Lehninger, A.L., and Hendler, R.W.: Direct measurement of the initial proton extrusion to oxygen uptake ratio accompanying succinate oxidation by rat liver mitochondria. *Biophys. J.*(in press).

Shrager, R.I.: Transformations and weights in biochemical curve-fitting. Georgetown University Med. Center, Dept. of Biochem., Wash. D.C., June 13, 1986.

Shrager, R.I., and Hendler, R.W.: Processing and analysis of potentiometric data. *Biophys. J.*49:687-691, 1986.

Tibbits, P.A., Boccuzzi, S.J., Sandquist, F., Bailey, J.J., Willems, J.L., Bourdillon, P.J., and Dreifus, L.S.: A comparison of the Bonner (V2MO) and Marquette 12 SL computer ECG programs. In Bailey, J.J. (Ed.): *Computerized Interpretation of the Electrocardiogram IX.* New York, Engineering Foundation, 1985, pp. 217-232.

van Rijk, P.P., and Bailey, J.J.: Nuclear cardiology. In van Rijk, P.P. (Ed.): *Nuclear Techniques in Medicine.* Den Haag, Nederland, Martinus-Nijhoff (in press).

van Rijk, P.P., Bailey, J.J., Bacharach, S.L., Bonow, R.O., Green, M.V., and Palmeri, S.T.: Computerized methods for detecting regional wall motion abnormalities using radionuclide ventriculography. *Eur. Heart J.* (in press).

Research Projects

Computer-Based Monitoring of the CNS in Critically Ill Patients

R.C. BURGESS

with: E.C. Jacobs, W.D. Hoffman (DCRT/LAS); CC/Critical Care Medicine.

Evaluation of the integrity and function of the central nervous system in critically ill patients who are comatose or who have some alteration of mental status currently cannot be done in an ongoing fashion. The purpose of this project is to develop and clinically test a computer-based system for acquisition, analysis, and display of scalp recorded neuroelectric signals (electroencephalogram and evoked potentials). This tool will be used to investigate the degree of dysfunction in neurologically impaired patients, to correlate the indices developed with other measures of cerebral function, and to evaluate the effectiveness of various therapeutic interventions.

Within the past year, automation of the entire process of patient stimulation, data acquisition, analysis, display, and archiving of results has been completed. The system automatically sequences from one stimulus modality to the next while simultaneously adjusting preamplifier/filter parameters and saving the results for trend analysis. Programs for digital filtering, frequency domain analysis, and color displays for highlighting important trends have been implemented. Normal volunteers have been studied using this system to determine normal ranges.

During the next few months the CNS monitoring system will be tested on dogs in conjunction with studies of septic shock by the Department of Critical Care Medicine. The results of the canine experiments will identify those parameters that are the most sensitive indicators of CNS function. These indicators will be combined into a CNS profile for further testing and validation on ICU patients.

Computer Systems for Nuclear Medicine

M.A. DOUGLAS

with: J.J. Bailey (DCRT/LAS); CC/Nuclear Medicine; NHLBI/CB.

This project involves computer-based mathematical analysis, pattern recognition, and image processing in support of diagnostic activities in the Nuclear Medicine Department of the Clinical Center and collaborating Institutes. Diverse applications include: computerized ECG-gated radionuclide ventriculography, myocardial perfusion scintigraphy, tagged monoclonal antibody studies, brain anatomy studies and pulmonary ventilation-perfusion relationships. Technical developments include: evaluation of the use of personal computers in nuclear medicine imaging; the specification and development of a new general purpose image processing facility for the Nuclear Medicine Department; and the development of methods to facilitate automated multimodality image registration of the head and other anatomy.

Multiple group logistic discrimination analysis has been performed on a test cardiac scintigraphy data base to determine the optimal minimum combination of parameters for the separation of the three groups (normal, focally abnormal, and diffusely abnormal) represented in the test population. A manuscript detailing the results has been accepted for publication. The optimal minimum parameter set that resulted from logistic discriminant analysis of the test population needs to be tested on a new, larger population. Acquisition of this population is proposed over the next few years if resources permit. When developed, this larger test population will be used in several cardiac scintigraphy research studies.

The file system of the new Nuclear Medicine Image Processing Facility has been fully specified and is being coded. The user interface and application system is currently being designed and specified. Head-holding devices necessary for multimodality registration have been designed, and are being tested, as is an x,y,z signal transducer. Systems capable of delivering ever increasing amounts of image data are continually being added to the Nuclear Medicine Department. Therefore, the development of fast interactive algorithms for the analysis of this data is a priority task, as is the related problem of multimodality registration.

Computer-Aided Analysis of Electrocardiography

J.J. BAILEY, M.D.
with: M.R. Horton, (DCRT/LAS); Framingham Heart Study; Georgetown Medical Center; Glasgow Royal Infirmary.

These studies are directed toward accessing the predictive accuracy of ECG criteria and the clinical utility of ECG computer programs. Further investigations involve the design of new criteria using well documented populations and statistical techniques.

In collaboration with NHLBI and Framingham study personnel, measurement data from the IBM program, echocardiographic measurement of left ventricle mass, age, sex and skin fold thickness from the Framingham study have been entered into SAS datasets. These data will be used to refine the left ventricular hypertrophy criteria for a stratified population. The Georgetown Medical Center data with infarct documented by autopsy have been used to test Marquette, IBM, and the Glasgow Royal Infirmary ECG programs. Two papers detailing these studies have been accepted for publication.

The refinement of left ventricular hypertrophy criteria based upon the Framingham data remains an important objective. The use of the Georgetown data to test additional programs, including those of Hewlett-Packard, Hannover, Duke, et al., also remains a project goal. However, progress in these projects is proceeding very slowly due to lack of support personnel.

Computer-based Analysis and Image Processing in Electron/light Microscopy and X-ray and Electron Energy Spectroscopy

M.A. DOUGLAS
with: S.P. Chock (NINCDS/LNC).

This project is directed toward the development of computer-based mathematical and statistical analyses, pattern recognition, and image processing of data, principally x-ray micrography and electron energy loss spectra, or from the electron/light microscopy images of biological specimens.

The Laboratory of Neurochemistry (NINCDS) is studying how granule swelling in mast cells and lifting of perigranular membrane occur during the exocytosis. They hypothesize de novo membrane generation as an integral part of the secretory mechanism of the mast cell. In support of this hypothesis, an objective analysis of the visual features in a large number of granules in a large number of mast cells in various stages of activation is being accomplished on the LAS minicomputer image processing system (DeAnza).

In a collaborative project with the Department of Neurosurgery at Children's Hospital, light microscopy is being used to study rodent spinal cords in order to determine parameters of injury (i.e., loss of axon volume, number of axons, inflammatory infiltrate, etc.). The number of specimens to be examined and the need for objective parameter estimation requires sophisticated image processing. A joint venture with LAS to assemble a video camera, digitizer, graphics adapter, and IBM PC-AT processor with appropriate software is in the initial stages.

Analysis of Physiological Signals

E.W. POTTALA
with: J.J. Bailey (DCRT/LAS); J.A. Dvorak (NIAID/LPD).

This project involves the development and application of minicomputer-based signal processing techniques for analysis of physiological signals (e.g., electrocardiogram, electromyogram, and electroencephalogram).

In the past this project has dealt with physiological signals from several diverse sources, such as ECG's from the Clinical Center and the Framingham Heart Study; blood pressure and ECG from a simian model of cardiovascular dynamics; and EMG's in occupational fatigue (NIOSH) and in myasthenia gravis (NINCDS). Development of the minicomputer-based system not only provided a high-quality general purpose analog to digital conversion facility, but also a variety of analog and digital filtering capabilities.

This year the focus has remained a collaborative project that was initiated in FY84 with NIAID to analyze ECG's in mouse models of Chagas' disease. The analog ECG's from that study have been processed and analyzed. A preliminary manuscript has been

submitted. Meanwhile the 16-year-old MAC-16 computer has encountered repeated failures and replacement parts for it are no longer available. Efforts to replace it with an LSI-11-based system are 60 percent completed. The LSI-11 system has many advantages over the old MAC-16 system. With this system it is now feasible to divide the ECG analysis package, which is currently implemented on the DEC-10 facility, into overlayed subpackages and convert them for the LSI-11 system. This overlayed system will reduce considerably the cost of analyzing animal ECG's.

Mathematical Models of Binding Equilibria

J.E. FLETCHER

The objective of this project is the study of mathematical models of ligand-receptor or ligand-macromolecule binding studies at equilibrium. Appropriateness of various model fitting criteria are studied and general guidelines and computational algorithms are designed for computer-aided interactive model fitting.

This project was not active in FY86, although requests for copies of exportable computer algorithms and reprints continue to be honored. The principal investigator will continue to serve as an occasional consultant, lecturer, and literature reviewer in this area.

Mathematical Modeling of Substate Transport in Physiological Environments

J.E. FLETCHER
with: R.W. Schubert, Louisiana Tech University/ Dept. of Biomedical Engineering.

Mathematical models of microcirculatory structure and function are developed from conceptual models into computer simulation models. The simulation model results are interpreted in terms of microcirculatory physiology. Project objectives are to study whole organ response and organ tissue level phenomena by means of mathematical models in an effort to determine relationships between variables that govern the organ response to physiologic challenges.

A major manuscript was revised in FY86 in compliance with editorial reviews. The revised manuscript was resubmitted. The loss of funding and reduction of personnel at the collaborating institution has curtailed laboratory investigations in this area. The future course of this activity is uncertain for FY87.

Mathematical and Computational Methods for Solving Nonlinear Equations

R.I. SHRAGER
with: NHLBI/LB; NIADDK/LCP; Behrooz Kamgar-Parsi, (DCRT/LAS); Univ. of MD/Comp. Sci. Dept.

Methods are developed for solving nonlinear equations frequently encountered at NIH. These equations are usually encountered in the context of constrained nonlinear least squares problems or in the numerical solution of nonlinear differential equations. Related problems, such as asymptotic error analysis and the efficient treatment of sparse matrix systems, are also considered.

Improved methods involving singular value decomposition (SVD) for the analysis of potentiometric data were published this year along with new results about the cytochrome chain. Also published were new concepts about proton ejection from respiring mitochondria, made possible by digital filtering techniques developed here. These filtering techniques were also incorporated into a neurological monitoring system also developed here. A robust binary search procedure is being presented at the national meeting of the Society for Industrial and Applied Mathematics. A curve-fitter has been written in the PC-MATLAB language for use in laboratory applications. Its performance will be tested in FY87.

Dr. Behrooz Kamgar-Parsi tested a new line search algorithm for optimization, and wrote a paper, *Line search for the optimization of multivariate functions*, to be submitted for publication.

SVD will be used to detect the conformational changes of hemoglobin once new lab equipment is built. Some mathematical languages will become prevalent on NIH lab computers, and these will need local consultants to provide advice and supplementary software. Filtering,

root-finding and curve-fitting will continue to find applications.

The Solution of Reaction-Diffusion Systems in Biology

J.E. FLETCHER

This project consists of the development of numerical methods and mathematical software for the solution of partial differential equations describing dynamic physiological processes. Adaptive finite element techniques have been generalized and used for models of nerve conduction, oxygen transport in tissue, uptake of macromolecules into the lymphatic system, and in preliminary studies of subsurface contaminant flow. FORTRAN-coded packages implementing these and other techniques are available for use on the major DCRT computers.

A principal investigator on this project left for private industry in early FY85. The software is being maintained in an active status and has been moved onto the Vector Facility, but further research in this area is limited to testing software developed elsewhere.

This project will remain active only at a minimal level until new technical staff can replace the principal investigator.

Applications of Personal Computers to Laboratory Research

M.R. HORTON

with: R.C. Burgess, M. Douglas, J. Fletcher, R. Shrager (DCRT/LAS); Personal Workstation Office (DCRT/OD).

The goals of this project are to determine the applicability of personal computer-based systems in research laboratories, to assemble such systems, and to test them in laboratory investigations. Because the technological advances in microcomputer architecture are occurring so rapidly, the peripheral equipment and software needed for laboratory applications continue to appear on the market in explosive fashion. The evaluation and selection of available, useful equipment and software for the development of microcomputer-based laboratory systems are undertaken in this project.

During FY86 the four LAS personal computer systems continued to serve as a basis for discovering appropriate application of microcomputer technology in the biomedical research environment. Emphasis shifted from hardware to software as various commercial packages were evaluated. These include a number of graphics and imaging packages, data base packages, and mathematical and statistical packages. The capability of personal computer systems to provide adequate imaging functions in the scientific environment improved during this year, but still awaits the next major hardware advance to realistically be competitive with more expensive systems. Data base usefulness was increased by the addition of software to perform simple statistical computations. The mathematical software MATLAB was upgraded during the year, and is being carefully evaluated for its usefulness in various applications, including curve-fitting, data manipulation, mathematical modeling, and singular value decomposition.

It is expected that the necessary hardware for satisfactory image processing on PC's will become available during the next year. This will lead to greatly increased use of the PC's for a number of imaging applications. The development of data analysis systems utilizing both the mainframe and the PC, with the LAN as a communicating mechanism, has begun and will be carried forward during the coming year. The use of the PC with appropriate mathematical analysis software will be promoted as an alternative to mainframe software that is becoming obsolete. In addition, newly developed hardware and software will be acquired subject to funding constraints with the objective of making the PC a more useful data analysis tool in the laboratory environment.

M. Horton serves as dBASE III consultant through the PWO and in the User Resource Center; M. Douglas serves as imaging consultant through the PWO.

VMAP enables researchers and typists to print scientific text, tables, and some diagrams on a laser printer, by preparing WYLBUR input files containing text and codes. The examples show the input file contents and the resulting printed output. VMAP was developed by LSM staff.

```
INPUT  ... of 138La using a La2O3 source[12,13].  They have
                                                          $
       presented 3.10*1011 yr for the partial half life
                                                          $
       of 138La b- decay by combining ...
          g' $
```

```
OUTPUT ... of ¹³⁸La using a La2O3 source[12,13].  They have
       presented 3.10×10¹¹ yr for the partial half life
       of ¹³⁸La β⁻ decay by combining ...
```

```
INPUT  ... let C(X,A) = z.  Then for g:X * A-->A there
                                                  $
       exists g:AX-->AX such that gp = g and ...
```

```
OUTPUT ... let ℭ(X,A) ≠ ∅.  Then for g:X ∩ A⟶A there

       exists g̃:A_X⟶A_X such that g̃π = g and ...
```

```
INPUT  1-------------------------------------------------------3
       |                                                       |
       |          n  f(k)(a)            x (x-t)n               |  (modifier
       | f(x) =   + [-------(x-a)k] + +  ------ f(n+1)(t) dt.  |   lines not
       |         k=0   k!                a   n!     1---------6|   showed)
       |                                           |Taylor series|
       7-------------------------------------------8------------9
```

```
OUTPUT
```

$$f(x) = \sum_{k=0}^{n} \left[\frac{f^{(k)}(a)}{k!} (x-a)^k \right] + \int_a^x \frac{(x-t)^n}{n!} f^{(n+1)}(t)\, dt.$$

Taylor series

Laboratory of Statistical and Mathematical Methodology

James E. Mosimann, Ph.D., Chief

The Laboratory of Statistical and Mathematical Methodology (LSM) combines research in mathematical statistics, mathematics, and computer and information science with collaboration and service in these areas for NIH researchers and administrators. LSM staff interact with all NIH Institutes, with other Federal agencies outside HHS, and with biomedical researchers worldwide.

In addition to the position of Chief, the laboratory has twelve full-time professional positions distributed among four sections:

- **Statistical Software Section** (SSS) provides consultation to and collaboration with NIH researchers and administrators in all computational aspects of biomedical data analysis, including selection and support of large systems and packages. Three specialists in scientific programming are led by a computer systems periodate oxidized nucleosides to proteins.
- **Statistical Methodology Section** (SMS) works closely with the Statistical Software Section. Three professionals in mathematical statistics, assisted by a staff fellow and a computer systems analyst, provide biostatistical consultation and DNA analysis software tools, and do independent research.
- **Biomathematics and Computer Science Section** (BCS), directed by a mathematician, with a computer specialist, performs independent research and provides consultation in mathematics and on software used for scientific printing and graphics.
- **The Medical Information Science Section** (MIS) investigates and develops methods for application of information and computer science to medical language data processing. A computer specialist works under the direction of the Chief, LSM. Another computer specialist is currently detailed to BCS.

Computation in FY86

A major part of LSM activity is the offering of statistical, mathematical, and other scientific systems and packages to the NIH user community. LSM staff evaluate new systems and packages for suitability and for response to needs at NIH.

LSM support always includes maintenance of the system or package, with adequate documentation, through NIH computer system changes, system or package updates, and corrections. It also includes rapid response to queries concerning user access to the most used systems and packages, including job control language, program parameters or other operating system procedures, and assistance in interpretation of results.

LSM recognizes the importance of teaching the effective use of systems and packages to biomedical researchers and other NIH users, and maintains a substantial program of short courses, documentation preparation, and informational talks and articles.

Computer systems and packages supported by LSM are shown in Table 1. Use of these statistical packages at NIH since 1975 is shown in Figure 1.

As in previous years, SAS is extensively used at NIH, with 85,000 IBM/System 370 accesses this month, up from 79,000 accesses per month one year ago. LSM taught eight introductory courses for SAS, and three courses for SAS/GRAPH. The SSS staff answered over 9,500 calls for statistical package assistance, mostly for SAS assistance. The average number of accesses per month for SPSS and SPSS-X was around 4,400, down from 4,600 per month in FY85. The BMDP package averaged 1,100 accesses, down from 1,200 in FY85.

Other software has more limited use--from an estimated 2,000 GRAPH sessions, 500 MLAB sessions, and 350 VMAP accesses per month, down to relatively few sessions for specialized programs such as REDUCE and a new product, DNALAB. DNALAB is used interactively in conjunction with laboratory studies of DNA, and can be used to display restriction enzyme cutting sites for cloning experiments, or possible splicings for coding exons. (Both DNALAB and VMAP are still under active development by laboratory staff.)

Support at NIH for the GLIM and CART statistical packages began late in FY86.

LSM teaching activities included courses in SPSS, BMDP, and VMAP, along with a seminar on GRAPH.

Table 1. Systems and Packages Supported by LSM.

SAS (Statistical Analysis System), SAS/GRAPH, SAS/ETS, SAS/OR, SAS/FSP
Vendor: SAS Institute, Inc. A batch and interactive IBM S/370 system for statistical analysis, with extensive file manipulation capabilities and graphics, also in interactive mode on the IBM PC-XT or PC-AT.

SPSS-X (Statistical Package for the Social Sciences, Extended), SCSS, SSPS-PC
Vendor: SPSS, Inc. A system for univariable and multivariate statistical analysis with file handling capabilities, in batch mode on the IBM S/370 and DEC-10, and interactive mode on IBM S/370, DEC-10 and IBM PC-XT or PC-AT.

BMDP (UCLA Biomedical Computer Programs), BMD
Vendor: BMDP Statistical Software, Inc. A collection of IBM S/370 batch programs for univariate and multivariate statistical analysis.

P-STAT (Princeton Statistical Package)
Vendor: P-STAT, Inc. A system for statistical calculations and file manipulation, in interactive or batch mode on the IBM S/370.

IMSL (International Mathematical and Statistical Libraries)
Vendor: IMSL, Inc. An extensive collection of FORTRAN routines for statistical and mathematical analysis, for IBM S/370 or DEC-10 batch computation.

MSTAT 1
Source: DCRT staff. IBM S/370 batch programs and subroutines for mathematical and statistical analysis.

GLIM (Generalized Linear Interactive Modeling)
Vendor: Numerical Algorithms Group, Inc. An IBM S/370 batch and interactive system for analysis of linear statistical models.

CART (Classification and Regression Trees)
Vendor: California Statistical Software, Inc. An IBM S/370 batch and interactive system for tree-structured regression and classification analysis.

GRAPH
Source: LSM staff. An interactive DEC-10 program for preparing a wide variety of graphs of scientific data.

DNA:DRAW
Source: LSM staff. An interactive DEC-10 program for preparing publishable displays of DNA sequences.

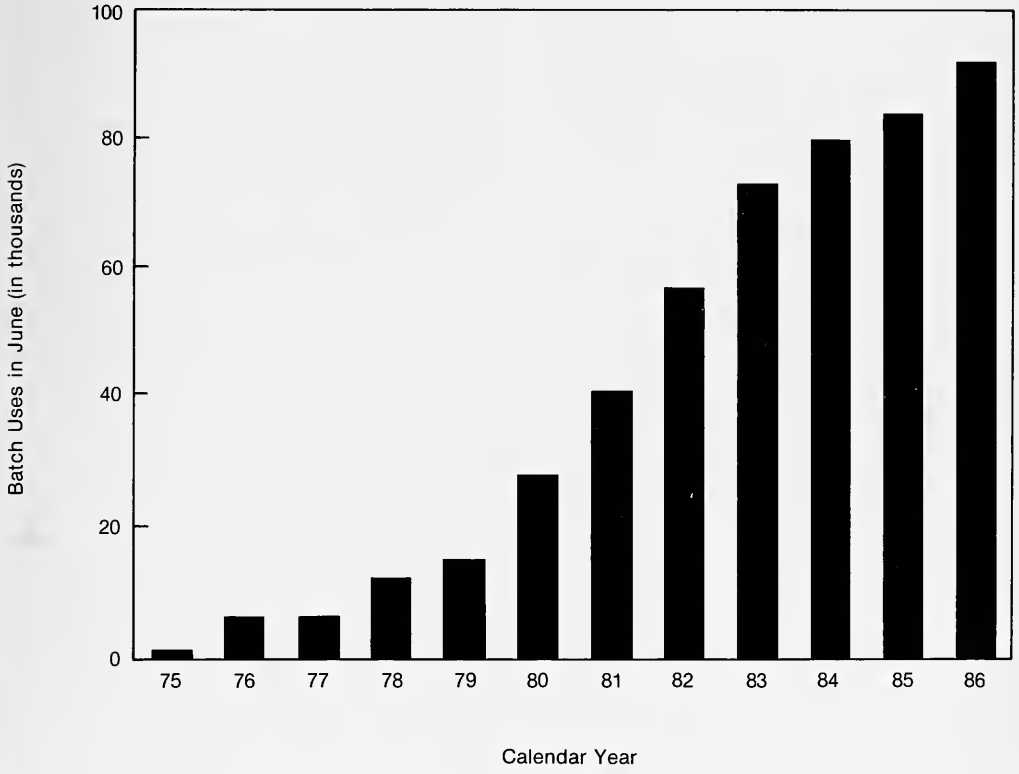
DNALAB
Source: LSM staff. An interactive DEC-10 program for graphically displaying effects of restriction enzymes in cloning experiments, locating possible exon splicing sites, and analyzing DNA sequences available from data banks.

MLAB (Modeling Laboratory, including C-LAB)
Source: DCRT staff. An interactive DEC-10 system for curve-fitting and analyzing functional or differential equation system models, with many cluster analysis and other mathematical operators, and publication quality graphics.

VMAP
Source: LSM staff. An IBM S/370 batch program used for printing scientific text and diagrams. It is used in conjunction with the WYLBUR text editor and IBM 6670 laser printers.

REDUCE 3
Source: Rand Corp. An interactive DEC-10 system used for symbolic and algebraic manipulation of mathematical formulas.

Figure 1. Use of Statistical Packages Supported by LSM/SSS.



Consultation, research collaboration in FY86

The staff of the Statistical Methodology Section provides consultation in a wide range of scientific fields, with interpretation of the results of statistical and other scientific computation. Some consultations are very brief because there is a known answer to the question at hand. Other consultations involve extensive time, and statistical or other scientific research. Research projects in LSM vary widely; they include studies employing statistical methodologies for biomedical applications, studies of language processing for medical information systems, studies of scientific computer printing and graphics, and research in mathematical and statistical methods.

During FY86, studies of size and shape variables were continued. These studies provide methods for studying random proportions or ratios of common occurrences in biomedical data. A paper on application of lognormal distributions to questions of size and shape was accepted for publication. A general class of distributions for the modeling of ratios and proportions was developed. Work is continuing on a general theory for modeling the correlational structure of proportions and its specialized computer program implementation. The Chief, LSM, visited the Facultes Universitaires Notre-Dame de la Paix, Namur, Belgium, for a six-month period of research.

In other work, the problem of optimal unbiased estimation for variance components in any mixed model has been fully resolved for the case where optimal means minimum variance. The techniques involved are quite algebraic in nature and this has led to the study of the algebraic structure of variance component estimation in general. Many of the important remaining estimation questions are thus shown to be reducible to ones involving algebraically simpler objects. These results now appear in a book, presently being reviewed for publication by Springer-Verlag, that also contains all the necessary algebraic background material needed to make these techniques accessible for the practicing research statistician in the biomedical community.

Research in nonparametric statistics with applications to biomedicine continued. A large-sample theory for weighted U-statistics has been developed and applied to a biomedical project and confirmed with a computer simulation. The study of the estimation of a paired difference in the presence of randomly missing data is being developed.

A collaborative study was completed with Dr. J. Hoofnagle (NIDDK/DD). Patients with primary biliary cirrhosis of the liver participated in a randomized trial to evaluate the drug chlorambucil. LSM provided nonparametric analyses to study the drug effects. Statistical procedures including tests for ordered alternatives and stepwise multiple comparisons were employed to evaluate the effect of the drug, using repeated measurements of bilirubin and serum immunoglobin levels, as well as percutaneous liver biopsy data. A coauthored article reporting the study has been accepted for publication.

In computer science, work is continuing on methods of computer generation of scientific text and graphics. It is expected that results of this research will be incorporated in an expanded version of the VMAP scientific printing package when more advanced printers become available for users of the NIH Computer Utility. Mathematical research on rings and modules continued. A project on the structure of Boolean algebras will be terminated with the departure of the principal investigator.

Research in medical linguistics continued. One area of study includes development of paraphrasing rules for Greek and Latin compound words and medical noun phrases, and development of single word segmentation procedures based on phonemic cues. A separate project for development of comprehensive lexicographic data base software continued; this software would facilitate merging of dictionaries, construction of microglossaries, and systematic accumulation of medical linguistic information. With the Laboratory of Pathology, NCI, and the DCRT Data Management Branch, LSM continued collaboration for improvement of the Clinical Center surgical pathology report data base and the associated report processing.

Collaboration also continued with Dr. E. Jaffe on problems of natural medical language data processing.

More Contract Support, Future Development

Laboratory service and research will be maintained as availability of staff permits. Some research projects will be discontinued because of the principal investigator's departure from LSM. Current levels of systems/ packages support, consultation and user assistance will be maintained as much as possible. During the current year, negotiations have been undertaken for contract support of various efforts related to MLAB, and continuing contract support of MLAB is planned. Further development of DNALAB and VMAP is anticipated.

Publications and Presentations

Campbell, G.: Comment on Size and Shape Spaces for Landmark Data in Two Dimensions. *Statistical Science* (in press).

Campbell, G.: Weighted One-Sample U-Statistics. Conference on Weighted Distributions, University Park, Pennsylvania, November, 1985.

Campbell, G., and Mosimann, J. E.: Models of Continuous Proportional Data Based on Functions of the Dirichlet Distribution Parameters, with Applications to Size and Shape. International Biometrics Conference, Seattle, Washington, July, 1986.

Campbell, G., and Skillings, J. H.: Nonparametric Stepwise Multiple Comparison Procedures. *Journal of the American Statistical Association* 80: 998-1003, 1985

Darroch, J. N., and Mosimann, J. E.: Canonical and principal components of shape. *Biometrika* 72: 241-252, 1985.

Dunham, G.: The Role of Syntax in the Sublanguage of Medical Diagnostic Statements. In Grishman, R., and Kittridge, R. (Eds.): *Proceedings of the Conference on Sublanguages* . Hillsdale, NJ, Lawrence Erlbaum Associates, 1986, pp.175-194.

Hoofnagle, J. H., Davis, G. L., Shafer, D. F., Peters, M., Avigan, M. I., Pappas, S. C., Hanson, R. G., Minuk, G. Y., Dusheiko, G. M., Campbell, G., MacSween, R. N. M., and Jones, E. A.: Randomized Trial of Chlorambucil for Primary Biliary Cirrhosis. *Gastroenterology* (in press).

Hutchinson, G.: Looking at Modules from the Outside. Mathematics Colloquium Lecture at George Mason University, November, 1985.

Hutchinson, G.: Representations of additive relation algebras by modules.*J. of Pure and Applied Algebra*42: 63-83, 1986.

Kuroiwa, T., Cahn, R., Juhler, M., Goping, G., Campbell, G., and Klatzo, I.: Role of Extracellular Proteins in the Dynamics of Vasogenic Brain Edema. *Acta Neuropathologica* 66: 3-11, 1985.

Mosimann, J. E., and Campbell, G.: Applications in Biology: Simple Growth Models. In Edwin L. Crow and Kunio Shimizu (Eds.): *Lognormal Distributions: Theory and Applications.* Marcel Dekker (in press).

Senapathy, P.: Origin of Eukaryotic Introns: A hypothesis, based on codon distributiion statistics in genes, and its implications. *Proc. Nat. Acad. Sci.* 83: 2133-2137, 1986.

Senapathy, P., Ali, M.A. and Jacob, T.M.: Mechanism of coupling periodate oxidized nucleosides to proteins. *FEBS Lett.* 190: 337-341, 1985.

Senapathy, P., Jayabaskaran, C. and Jacob, T.M.: Purification of antibodies for the cytokinin N(6) (Delta Square - isopentenyl) adenosine by affinity chromatography. *Nucleic Acids Res.* 13: 5833-5842, 1985.

Shapiro, M. B.: Draw Your Own Publication Quality Graphs--Using the Computer. DCRT/LSM Seminar, November, 1985.

Shapiro, M.B.: Poster sessions on DNALAB and DNADRAW at international meeting on Problems in Genetic Sequence Analysis. Waterville, NH, August, 1986.

Shapiro, M. B., Schein, S. J., and DeMonasterio, F. M.: Regularity and structure of the spatial pattern of blue cones of macaque retina. *J. Amer. Stat. Asso.* 80(392): 803-814, Dec. 1985.

Shapiro, M. B., and Senapathy, P.: Automated preparation of DNA sequences for publication. *Nucl. Acids Res.* 14(1): 65-73, 1986.

Sinclair, D. F., Mosimann, J. E., and Meeter, D. A.: Tests for character displacement. *Biometrics* 41(4): 835-846, 1985.

Sinclair, D. F., Mosimann, J. E., and Meeter, D. A.: Tests for deletion. *Biometrics* 41(4): 847-857, 1985.

Research Projects

Automated Data Processing of Medical Language

M. G. PACAK,Ph.D.
with: A. W. Pratt,M.D. (DCRT/OD); G. Dunham , S. Harper (DCRT/LSM); E. Jaffe (NCI/DCBD); D. Henson (NCI/DCPC).

The major objective of the project is the development of methods for the automatic processing of natural medical language. This involves both development of algorithms for parsing and representing natural text, and creation of computer dictionaries and other data bases for medical specialties such as surgical pathology.

Research in medical linguistics continued, including the development of paraphrasing rules for compound terms derived from Greek and Latin. Patterns of paraphrasing rules for medical noun phrases were prepared. Formalization of the concept of a merge of incompatible medical dictionaries was studied. Methods were studied for a single word segmentation procedure based on phonemic cues, independent of semantic or lexical computation, which would accurately segment words containing semantic, derivational, and inflectional morphemes.

Collaboration continued on the Clinical Information Utility with the Laboratory of Pathology, I/DCBD, and W. Douglas Vincent, DCRT/DMB, in using LSM's automatic encoding system to maintain and improve the data base of Clinical Center surgical pathology reports. A new version of the encoder allowing full use of available Medical English syntactic information was tested and put into routine service. Together with Dr. Thomas L. Lewis, CC/IS, we provided advice on modernization of report processing for the Laboratory of Pathology.

Conversion to IBM 3480 format magnetic tapes and projected replacement of ISAM by VSAM IBM System 370 disk access methods has necessitated substantial conversion and modification of the Pathology Retrieval Information System and its dictionaries. Work is continuing.

Development of the Lexicographic Environment Software continued. This package provides medical lexicographers with a comprehensive lexicographic data base to study and maintain the vocabulary and lexicographic relationships within dictionaries and to create new relational structure in them. The system design provides for the representation of structure as partially-ordered sets or trees, the display of differences and similarities among sets of dictionaries, the merging of dictionaries, and the construction of microglossaries. It facilitates systematic accumulation of morphosyntactic, morphosemantic, orthographic, semantic, definitional, and distributional information about medical words, phrases, and discourse.

Research in computational linguistics, current collaborative efforts, and development of the Lexicographic Environment Software will continue.

Cluster Analysis

M. B. SHAPIRO

The main objective of this project is the application of computer cluster analysis and related methods to NIH research problems.

Computer techniques for assisting recombinant DNA research were developed. A software package, DNALAB, for interactive use in conjunction with laboratory studies of DNA, was made available to NIH computer users. It features graphical output showing the effect of using specified restriction enzymes in a cloning experiment, and enables a researcher to select an optimum combination of such enzymes to achieve a desired clone. DNALAB also provides graphically displayed information showing the location of possible sites where the protein coding exons are spliced together. In addition, DNALAB contains a number of standard options found in other current DNA software.

Development of DNALAB as a research tool is continuing.

Discrete Mathematics and Applications

G. HUTCHINSON, Ph.D.

The project objective is to develop mathematical theory and computational techniques using discrete mathematics (algebra, combinatorics and graph theory), and to apply such methods to appropriate problems of biomedical research and computer science.

New conditions characterizing existence of exact embedding functors between categories of modules have been found. Two of the shorter results were submitted for publication.

In previous work under this project, the VMAP system for describing scientific text was developed. During FY86, design of a more powerful version of VMAP was completed. This design makes available to users many more fonts, special characters, and facilities for increased control of printed scientific output. It also makes it easier to describe complex formulas, tables, and diagrams in many cases.

Analysis of categories of modules will continue. Preparation of computer programs and documentation for release of the new VMAP design will proceed, depending upon the availability of printing facilities suitable for scientific text.

Multivariate Statistical Analysis

J. E. MOSIMANN,Ph.D.
with: G. Campbell,Ph.D. (DCRT/LSM).

The objective of this project is the study of multivariate ratios or proportions.

Studies of random proportions that follow mixtures of Dirichlet distributions were continued, and the results will be presented at the International Biometrics Conference in Seattle during this fiscal year. Several papers previously in press appeared, two in *Biometrics* and one in *Biometrika*. Studies relating size and shape analysis with Correspondence Analysis, and other generalizations of Principal Component Analysis, were initiated while visiting the Facultes Universitaires Notre-Dame de la Paix, Namur, Belgium.

Present research studies are being undertaken with a view toward writing a monograph on the subject.

Linear Methods in Statistics

J. D. MALLEY, Ph.D.

The objective of this project is to study new algebraic methods in statistics and their applications to biomedical research.

Additional results have been obtained and consolidated for the problem of optimally estimating the variance components in an analysis of variance. These new methods fully solve a part of the general estimation problem and, where applicable, are easy to calculate. These methods are algebraic in nature and bring to statistics a new point of view. The ideas and techniques have been introduced in a completed book, which is now in the publisher's review process. The text is written in a self-contained manner, which leads the biomedical researcher step by step to the latest results. Because all necessary algebra is included and the statistical purposes are clearly detailed, the techniques are accessible to biostatisticians. Methods are given for optimal unbiased estimation of the variance components, in any mixed model with arbitrary kurtosis and unbalanced data.

Nonparametric Statistics

G. CAMPBELL, Ph.D.

Research in nonparametric statistics with applications to biomedicine continued. A paper with J. H. Skillings on nonparametric multiple comparisons has appeared. A large-sample theory for weighted U-statistics has been developed and applied to a biomedical project, and confirmed with a computer simulation. The study of the estimation of a paired difference in the presence of randomly missing data is being developed.

The study of proportions is being continued. A general class of distributions for the modeling of ratios and proportions has been developed. Work is continuing on a general theory for modeling the correlational structure of proportions and its specialized computer program implementation. These developments have many applications to biomedical data expressible as proportions.

Computer Graphics and Mathematical Applications

K. R. BHUTANI, Ph.D.

The major objective is to formulate mathematical and computational techniques, and to apply them to problems of biomedical research and computer science.

Research during FY86 was concentrated on Boolean algebras and abelian groups in a topos of sheaves on a locale. In particular, the notion of stability and related topics was studied. A paper on this research has been submitted. Two more manuscripts on the study of injectivity and essential extensions of abelian groups have been submitted.

Development of procedures using REDUCE for symbolic and algebraic calculations was continued.

This project will be discontinued at the end of the fiscal year due to the departure of the principal investigator.

DNA Sequence Analysis and Related Methods

P. SENAPATHY, Ph.D.

DNALAB, a comprehensive software package dedicated to aiding recombinant DNA research, has been developed. This package contains, in addition to standard options available in related software, several unique features for sequence analysis. One of the options allows a researcher to identify the restriction enzyme sites closest to a given range of sequence, where the enzymes generate an easily separable

fragment that includes the range. Another option enables one to analyze potential splice sites in a gene sequence, delete the hypothetical introns, and analyze the mRNA sequences possible from such splicing.

Extending DNALAB, a program PROFIND is being developed in order to automatically identify possible protein sequences coded for from an eukaryotic gene sequence. This is done by first finding the various potential exons by using several criteria, splicing them in all possible combinations, and rating the resulting mRNAs and proteins based on several parameters found in actual coding sequences of eukaryotic genes. This capability would be very useful, because there seem to be many more proteins coded for from an eukaryotic gene sequence than currently identified in the laboratory due to insufficient experimental sensitivity. The potential mRNAs and proteins found by computer would enable scientists to design laboratory experiments to identify them.

The consensus signal sequences at the site of gene splicing in a eukaryotic coding gene are being analyzed by counting the nucleotide frequencies at these sites from databank sequences using the computer. Very interesting variations are observable between different classes of organisms in the consensus signals; these differences may have evolutionary meanings.

There seem to be short stretches of sequences within the intron sequences of an eukaryotic gene that serve as signals for the splicing machinery in order to correctly splice the exon sequences together. A program, SIGNAL, has been developed to identify consensus signals from a given set of similar sequences. With SIGNAL, the consensus sequences within introns are currently being identified. Being able to identify these signals will aid understanding the mechanism of splicing as well as the evolution of the splicing signals and the splicing machinery.

In another area of research, further computer studies have extended the theory recently proposed by this researcher for the possible evolution of prokaryotes from the primitive unicellular eukaryotes to that of yeasts, a class of simpler unicellular eukaryotes. The results indicate that yeasts could not have evolved from prokaryotes (in contrast to the current general thinking), but could have evolved from more ancient unicellular eukaryotes (containing a full complement of introns) by losing some of the introns in their DNA. Further, these studies indicate that mitochondria could not have originated as endosymbiotic bacteria, as currently thought. It seems that mitochondrial genes originated from nuclear or nuclear-like genes and formed a separate energy-organelle mitochondrion due to some evolutionary advantages.

Algorithms and Other Methods for Biomathematical Computing

J. POCHOBRADSKY, Ph.D.

The major objective of this project is to develop computer algorithms and methods that are useful in biomathematical analysis or display of biomedical data. Implementation of these methods in MLAB is usually under consideration.

A system for easily obtaining three-dimensional graphics of certain kinds was implemented using MLAB. These procedures permit stereo views and other special views to be generated with automatic computation of the necessary parameters.

In conjunction with the testing of the IBM 3090 array processor at NIH before IBM made the product announcement, discriminant analysis algorithms were translated from PL/I to FORTRAN and tested in scalar and vector processing modes.

This project was terminated during the fiscal year due to the departure of the principal investigator.

Consulting Services

J.E. MOSIMANN, Ph.D.
with: James D. Malley, Ph.D. Gregory Campbell, Ph.D. Marvin Shapiro, P. Senapathy, Ph.D. and Jiri Pochobradsky, Ph.D. (DCRT/LSM).

LSM staff members provide consulting services in statistics, biomathematics and computer analysis of DNA sequences. Brief descriptions of LSM consultation work are given below.

Dr. M. M. Mourandian (NINCDS/ET): Efficacy of intravenous infusion of sinemet for the treatment of

Parkinson's disease was studied, in a group of patients for which the tradational drug delivery methods have become ineffective. Of particular interest was the study of the reduction in the fluctuations (variance) of the patient response, as well as the overall improvement. LSM provided assistance on the statistical analysis.

Dr. Anthony Luger (NINCHD/DEB): Relationships between stress and hormone levels were studied. Three groups of people were placed in exercise training programs of different intensities, and estimates were also made of their basic resting work levels. Hormone levels were then measured over time, and a multifactor repeated measures, with unbalanced data was performed. Suggested techniques included statistical methods developed by Dr. James Malley (DCRT/LSM) for unbalanced multivariate analysis of variance.

Dr. Gordon Cutler, Kevin Barnes (NICHD/DE): Long-term relationships between hormone levels and early puberty in children are being studied. LSM assisted in statistical analysis involving an unbalanced profile analysis and analysis of variance with covariate adjustments, in an effort to separate normal growth components from abnormal developments.

Dr. S. H. Wollman (NCI/LMBGY): The structure of thyroid follicle cells in rats injected with Thyroid Stimulating Hormone is investigated. LSM provided advice on statistical techniques and simulation based on stereological principles.

Dr. R. A. Brooks (NINCDS/IR/OD): The statistical relationship between the cerebral glucose metabolic rate and an index of brain size are measured by PET scans of normal human volunteers. LSM assisted in use of statistical techniques to study the relationship of these two variables.

Dr. H. Kruth, J. Cupp (NHLBI/EA): The build-up of foam cells on the interior walls of the hearts of swine is measured by flow cytometric techniques. LSM provided the nonparametric statistical analysis for two studies of the build-up of foam cells.

Dr. J. Hoofnagle (NIDDK/DD): Patients with primary biliary cirrhosis of the liver participated in a randomized trial to evaluate the drug chlorambucil. LSM provided nonparametric analyses to evaluate the effect of the drug.

Dr. A. Cheever (NIAID/LPD): Schistosomiasis infections of different strains of mice by different parasite strains are studied. LSM assisted in data base management for experimental measures of levels of fibrosis, granuloma size, and size of infection, and provided advice and assisted in statistical analyses.

Dr. R. C. Chen (NIHLBI/IR/LC): Studies in suppression of certain kinds of drug toxicities by addition of GSH to cells continued. LSM continued to assist in using MLAB to formulate and analyze complex pharmacokinetical systems of equations modeling the system.

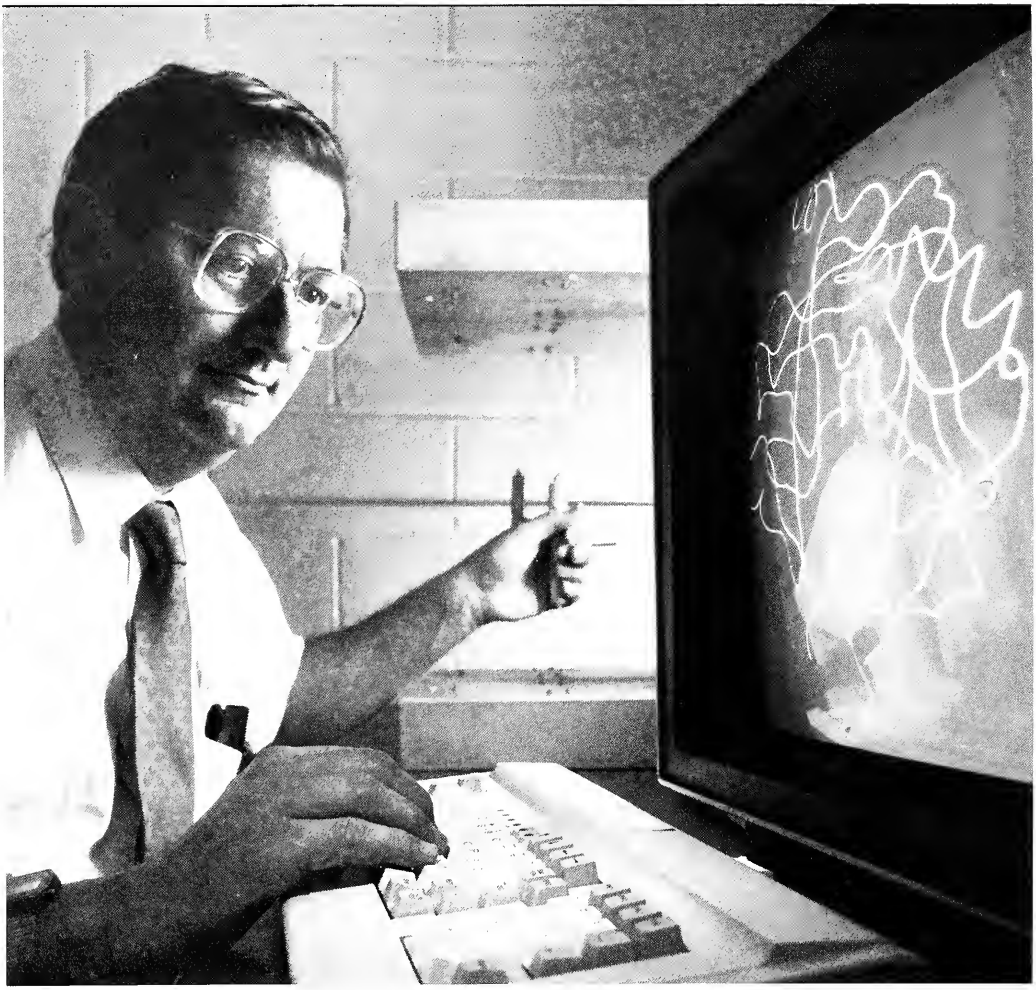
Dr. J. van de Geijn, R. Creecy (NCI/DCT/RO): Radiation doses in human patients are estimated by measurements made in water targets. LSM assisted in formulation and curve-fitting of analytical models, using MLAB.

Dr. R. Chatelier (NIDDK/LBP): Sedimentation of very concentrated solutions of two proteins is studied. LSM assisted in generation of 3-D stereo images comparing predictions of an analytical model with experimental data, using MLAB.

There were a number of brief consultations involving use of DNADRAW software to prepare displays of long DNA sequences for publication or presentation by slides. Consultations on the use of DNALAB for analysis of DNA sequence data have also been provided.

Consulting services will continue with available staff. Due to staff reductions, biomathematics consultation will be very limited.

The Office of the DCRT Director has a molecular and cellular graphics research component that applies computing technology to biomedical research. Richard J. Feldmann used the capabilities of molecular mechanics and graphics programs as they developed this year to initiate a project aimed at providing a tool for understanding the folding of proteins.



Office of the Director

Arnold W. Pratt, M.D., Director

The Office of the Director provides overall program and management direction for DCRT. The Director, Deputy Director, Assistant Director and Executive Officer work together as the immediate Office of the Director.

In addition, the Office of the Director is the central central NIH resource for advice and assistance on matters related to complex policy and procedures governing the procurement of computers in the Federal Government. It serves as the NIH point of contact on these matters with Federal agencies.

Also within the Office of the Director is the **Equal Employment Opportunity Office,** which manages a full EEO program for the Division. The office serves as the focal point and advisory for all activities relating to the equal employment opportunities of its employees and applicants. The EEO Officer maintains a close working relationship with the NIH Division of Equal Opportunity and other components concerned with minority and women's issues.

Four other offices supplement the work of the DCRT laboratories and branches:

- The **Personal Workstation Office** (PWO) provides guidance and technical assistance for the effective use of personal computers at NIH.
- The **Office of Administrative Management** (OAM) provides administrative and managerial support for the work of DCRT. OAM includes the Administrative, Personnel, Financial Management, and Project Control Offices.
- The **NIH ADP Policy Office** (NAPO) is the central NIH focus for advice and assistance on matters related to complex policy and procedures governing the management of computers under the Department's Information Resources Management (IRM) program.
- The **Office of Scientific and Technical Communication** (OSTC) serves as a central source of information about DCRT activities and about computing and related disciplines. It includes the DCRT Information Office and the DCRT Library.

The activities of these four offices are detailed in the next section of this *Annual Report.*

The Office of the Director also has a molecular and cellular graphics research component that applies computing technology to biomedical research.

Molecular Graphics

The Molecular Graphics section solves problems in macromolecular structure representation and modeling for collaborating NIH scientists and visitors. Five staff members (one computer specialist and four physical chemists) work in a laboratory with about 25 computers, which are organized into several networks so that they can communicate with each other. The work of the past few years has been to develop each type of computer so that it does one or more specific functions and thus forms a part of the wole system. Because the power of the computational and graphics system is apparent only in solving problems, they take on selected problems they are important in themselves but that also serve to develop an understanding of the behavior of the computing system.

Dr. Brooks implemented the molecular mechanics program CHARMM (Chemistry at HARvard Molecular Mechanics) on the Star Technologies ST-100 array processor. This work took almost a year but the results are very impressive. In actual timings, the program running on the array processor is 150 times as fast as a DEC VAX-780, twice as fast as a Cray-1S computer and almost as fast as the Cray XMP computer (the type of Cray computer often labeled as a Super Computer). This accomplishment means that individual laboratories can do molecular mechanics calculations for a very modest investment. It also readjusts the dynamic balance between super computers and laboratory computers.

Following a demonstration at the Molecular Graphics meeting in southern France, which was the first time the program ran on a machine outside NIH, Dr. Brooks exported the program to several laboratories in universities in the eastern U.S.

Dr. Pastor and Mr. Venable of the Bureau of Biologics, FDA, worked on the development of the simulation of membranes. Working first on the network of computers in the laboratory, they implemented programs that Dr. Pastor brought with him from his graduate studies. During the year they experimented with the programming of the array processor associated with the IBM 3090 computer in the NIH central computer facility. This array processor compares favorably with the laboratory array processor and for certain problems, particularly the manipulation of large matrices, it provides unique capabilities.

Dr. Lee of DCRT's Physical Science Laboratory worked on the development of a graphics program for the Silicon Graphics display. This work started with the realization that the existing programs dis not serve present and anticipated modeling needs. It meant going back to the beginning to develop the software infrastructure for the type of molecular modeling performed at DCRT.

Utilizing the capabilities of the molecular mechanics and graphics programs as they developed through the year, Mr. Feldmann initiated a project aimed at providing a tool for understanding the folding of proteins. The outcome of the UPATSU (Understanding Protein Architecture Through Simulated Unfolding) project will be a set of stereo slides of all the protein architectures. The slide set will be distributed to scientists throughout the world.

Several years ago when the implementation of the third molecular graphics system in DCRT began, we had the sense that the pace of technology was accelerating. Today we find it even more difficult to keep up with the pace of the changing technology. It is very difficult for scientists in any setting to buy and use computers that will clearly be superceded in a year or two.

In this generation we have struggled to bring graphics, stereo, three-dimensional Joystring control, array processor computation, voice input/output control and intellection together from separate components. The solution seems to be to attempt to influence the design cycle of the next generation of computers so that this next generation will have all the properties put together in the proper manner.

Publications

Hargrave, P.A., McDowell, J.H., Feldmann, R.J., Atkinson, P.H., Rao, J.K.M., and Argos, P.: Rhodopsin's Protein and Carbohydrate Structure: Selected Aspects. *Vision Res.* 24: 1487- 1499, 1984.

Research Project

Understanding Protein Architecture Through Simulated Unfolding

RICHARD J. FELDMANN
with: Bernard R. Brooks (DCRT/OD); B.K. Lee (DCRT/PSL).

Recent progress in sequencing proteins directly from the gene structure rather than by step-by-step degradation techniques has exponentially increased the number of available protein sequences. Where crystal structures for members of a protein family exist, suitable computer graphic models can be constructed. It is, with few exceptions, impossible to build a model directly from the amino acid sequence. This is true because in general we do not understand how proteins fold.

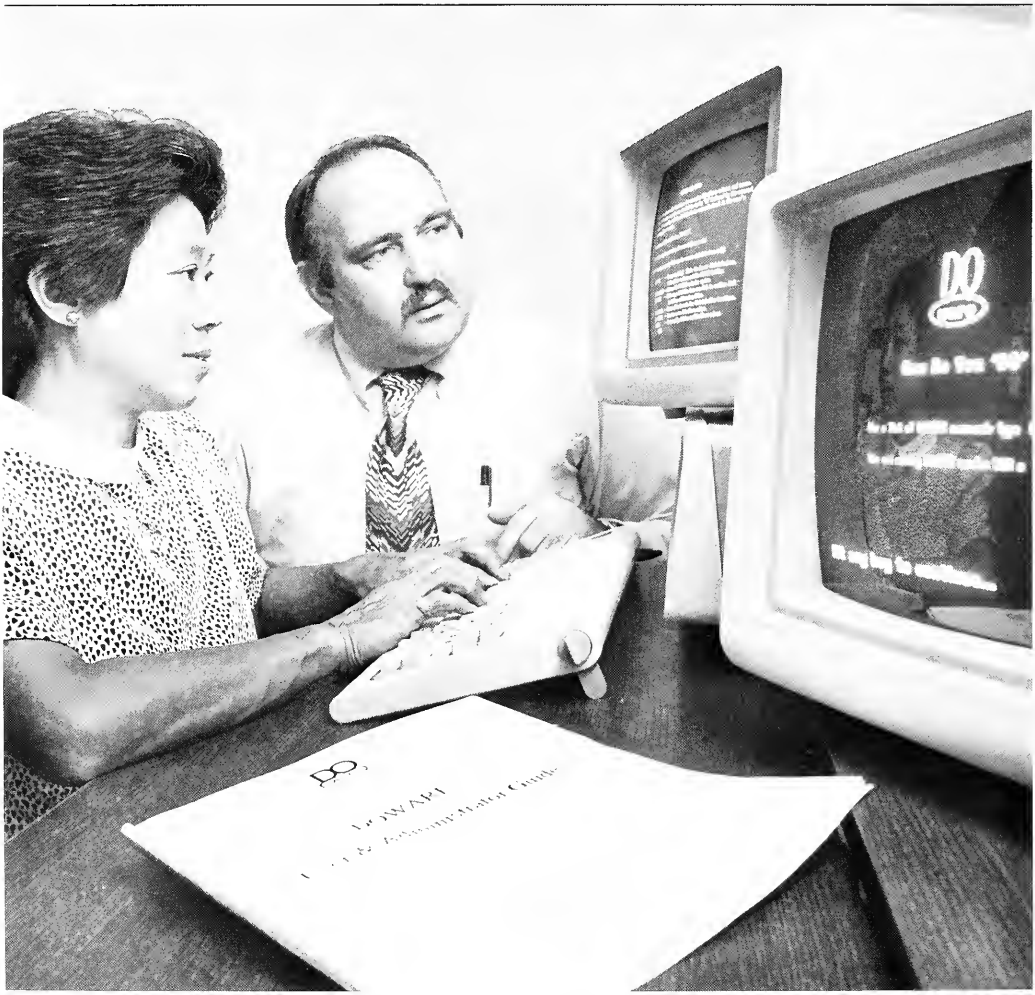
The understanding of the folding of a protein into a compact three-dimensional structure after synthesis by the ribosome has been slow to develop.

In looking at the currently popular computer representations of macromolecules, it became clear that there was some deficiency. The carbon alpha representation that uses one line segment per amino acid is too abstract and the lines change direction too sharply. The peptide backbone representation that uses three line segments per amino acid is too complex. We developed a procedure using CHARMM to smooth the peptide backbone. The result is a smooth space curve much like a piece of stiff wire. With this procedure we have processed all the protein data sets in the Protein Data Bank from the Brookhaven National Laboratory.

A set of stereo color slides has been prepared showing all of the proteins and their domains. The stereo slide set will be distributed to scientists throughout the world so that they can begin to think about the folding of proteins in a more graphic way.

In looking at the stereo slides it has become clear that there is a logic of protein folding. We are attempting to encode this logic using the Knowledge Engineering Environment from Intellicorp.

A Local Area Network (LAN) was installed to interconnect computer terminals, systems, and modems throughout DCRT in early FY86. James Del Priore then developed DOware—special software to provide easy access to the LAN, along with major new functions. Here, Del Priore demonstrates DOware enhancements to DCRT Lead User Ellen Chu.



Personal Workstation Office

David C. Songco, Chief

The Personal Workstation Office (PWO)provides guidance and support to scientists and administrators throughout the NIH in the effective use of personal workstations and associated automation technology. It provides technical assistance, training, and publications on relevant hardware, software, and overall personal workstation architecture. In conjunction with other DCRT labs and branches, the PWO collects, develops, and distributes software utilities of general use to the NIH community.

As part of the training and consulting function ,the PWO sponsors a User Resource Center (URC) in collaboration with the Division of Personnel Management (DPM) and the Division of Management Policy (DMP). The PWO works closely with the DCRT labs and branches to monitor the rapidly changing technology and the technical requirements of the user community in the area of personal workstations and the associated interfaces to the NIH Computer Utility so that these needs are accurately reflected in the development and support provided by DCRT.

Training, Assistance Aid Increasing PC users

The use of personal computers at NIH continued to grow during FY86 and with this growth came an increase in demand for support for PC users. The development of a centralized support group backed by specialists within DCRT combined with 185 Lead Users from 45 organizations across NIH proved to be an effective way to provide support for over 2,500 PC users.

Support for personal computer users at NIH begins with quality training. Through training, PC users become more knowledgeable in the use of personal computers and are better prepared to apply this technology in an effective and efficient manner. The PWO sponsored 15 different courses presented in 57 sessions during FY86 to over 1,200 registered students. Instructors for the lead user series and the open PC training were drawn from the PWO and from other DCRT labs and branches. Additional microcomputer training was provided by vendors at the URC. The PWO serves as technical consultant to DPM in the selection of vendors and course material. This collaboration ensures that both compatibility and support issues are considered in the selection of courses to be offered to the NIH community. The combined totals for microcomputer training offered by DCRT and DPM in FY86 show 97 total sessions presented to over 2,000 students.

The requests for quality training on the PC products supported by DCRT continued during FY86. In response to this demand and in line with the PWO policy of involving end users in the support effort, a PWO Associate Instructor Program was developed. Lead Users were trained to work with the main classroom instructor and assist students during the hands-on sessions. Several Lead Users also presented PC training in the URC to users within their organizations based on courses developed by DCRT.

User consulting and guidance is provided for NIH scientists and administrators who are experiencing difficulties using the personal workstation products supported by DCRT. This consulting is available by telephone and by direct visit in the NIH User Resource Center As part of this process PWO staff may refer clients to specialists in other DCRT labs and branches. BID Lead Users are also called upon to present demonstrations and assist in the consulting process. The PWO answers several hundred requests for assistance each month.

The concept of establishing working groups of NIH employees to focus on specific application areas was extended to include three new groups, for statistics, PC-assisted instruction, and DisplayWrite 3. The major goal of the statistical group is to match the statistical application to the appropriate statistical package. Meetings began in January and continued throughout the year. Evaluations of a variety of statistical packages were made available to the NIH community. The PC-Assisted Instruction Working Group was formed in May of this year to explore and evaluate training and testing applications using personal computers with interactive video and various other input/output devices such as a touch screen, light pen, joystick, mouse, and computer-generated voice. A PC DisplayWrite 3 (DW3) working

group began meeting in February. This group exchanges information on the use of DW3 at NIH.

This year the PWO instituted a self-maintenance program for repairing personal computers in response to the need for decreased cost and improved quality in service and repair. Under this program a one-day course is offered to NIH employees covering the diagnostic procedures required to identify specific malfunctions of the hardware products supported by DCRT. The user is also instructed in the proper procedures for replacing faulty components. Because of the modular design of the supported architecture, no special tools are required. Beginning in October 1986, spare modules will be available through the Biomedical Engineering and Instrumentation Branch (BEIB), DRS. Users can exchange faulty modules for replacement parts at a rate substantially below that charged by local service vendors. BEIB technicians will also repair supported hardware on a fee-for-service basis. Vendor service is still available from several sources.

Over 600 NIH employees attended the first NIH PC Software Fair held in May of this year. This two day event featured demonstrations of PC application software developed at NIH. The NIH Fair was different from other software demonstrations because it was planned and presented by NIH employees, rather than vendors, and because if focused on applications developed at NIH, rather than vendor products.

An updated PWO Utility Diskette was distributed to PC users at NIH. This diskette contains programs developed at NIH as well as other useful public domain programs.

An updated *PC Product Information Guide* describing the products supported by DCRT was distributed to PC users at NIH. A *PC guide for 3270 emulation* was also published to assist users in accessing DELPRO, DB2, and other full screen products offered by the NIH Computer Utility. The *PWO NEWSBRIEF* is published every eight to ten weeks. It has a six-page format and contains technical notes and information on meetings and other events of interest to PC users. Material for *NEWSBRIEF* is obtained from PWO staff, DCRT specialists, and users. It is designed to complement the DCRT *INTERFACE* with a focus on personal workstations and associated automation technology.

Collaboration with the Computer Systems Laboratory (CSL) and the Data Management Branch (DMB) in the investigation of LAN technology as it relates to personal workstations continued during FY86. The DCRT Ethernet is now serving 80 registered PC users across DCRT. This experience forms the basis for providing guidance to other NIH organizations interested in interfacing personal workstations via local area networks. As part of this service representatives from PWO, CSL, and DMB provide regularly scheduled seminars on this rapidly emerging technology. This seminar series coupled with the development of DO, a powerful yet easy-to-use set of network functions, is responsible for the wide acceptance of the Ethernet technology as an LAN solution at NIH. Details of the DO development are described in the Computer Systems Laboratory section of this *Annual Report*.

Tests of PC technology To Continue in FY87

The PC user training series offered in the URC will be enhanced with advanced courses offered for supported products. A second classroom will begin operation in FY87. This classroom will offer training tailored to the specific needs of NIH organizations. Training in this classroom will be provided on a fee basis by vendors screened by the PWO. The second classroom will be administered by the NIH Training Branch. The DCRT microcomputer lecture series will continue as an introduction to PC technology.

In collaboration with the Computer Center Branch and the Data Management Branch, the PWO will continue the development and testing of a reliable file transfer process for 3270-based applications including format conversions that will permit the efficient exchange of data between mainframe and local data bases.

The PWO is investigating the use of an Ethernet server that acts as a 3270 controller. This combination will permit Ethernet users to access the 3270-based

services provided by the NIH Computer Utility via Ethernet.

The PWO in collaboration with NIH scientists will investigate the IBM Token Ring technology as an alternate means for connecting personal workstations. This investigation will include the connection of the IBM PC-XT, the IBM PC-AT and the IBM PC-RT, a 32-bit personal computer designed for scientific applications. This project will complement the 32-bit PC development efforts of the Computer Systems Laboratory by focusing on commercially available products. The first application to be investigated is the use of laser technology printers for the production of scientific reports and documentation.

The consulting service will be enhanced by the addition of an online PC information retrieval system that will provide selective retrieval of technical reports, descriptions of supported hardware and software products, procurement information, and miscellaneous information acquired from applications developed at NIH via the NIH Computer Utility. It is hoped that this service will reduce the number of telephone calls for assistance. Users will logon to the DCRT WYLBUR system and activate WYLBUR command procedures by a series of menus.

Research Work

Personal Computer Implementation on Local Area Networks

R.J. ROMANOFF
*with:*J.S. Del Priore, W.L. Risso, Jr. (DCRT/CSL); B.R. Cole, J.R. Parks, Jr. (DCRT/DMB).

This is a collaborative project with PWO, CSL, and DMB to develop and to implement a plan for the connection and use of PC's on the DCRT Ethernet, and to investigate LAN technology as it applies to PC's in the NIH environment. The knowledge and experience gained will form the basis of advice given to other NIH organizations.

The DCRT Ethernet LAN was installed in early FY86 as the first step in developing expertise in LAN technology. The LAN interconnects many computer systems, terminals, and modems in use throughout DCRT. At the close of FY86 there were 70 users defined to the LAN. These users were distributed among two state-of-the-art high-capacity computers designed to be LAN servers and one PC-XT. During the FY86, the DOware program to interface the user to the network was developed by James Del Priore of CSL. This program provides easy access to the LAN for users and makes major new functions available.

A four station IBM PC Network was purchased so that familiarization with this different approach to LAN implementation could be explored.

The number of users defined to the DCRT LAN was increased to approximately 90, from 70 in FY86. DMB has replaced their PC-XT with a 3COM 3SERVER offering many more users expanded resources and increased performance. Use of the network ranges from heavy use of the interuser mail facility to storage and sharing of data generated from a wide variety of software packages. A high-speed letter-quality laser printer was added to one of the servers and is available for use by anyone logged into the network. The LAN now has five printers available for shared use.

The DOware software interface to the network was enhanced with many new functions designed to make efficient use of the LAN resources. During FY86, DOware was requested and installed in several LAN's at NIH similar to DCRT's. A comprehensive *Doware User and Administrator Reference Guide* was written and distributed to DCRT LAN users.

Many sessions were held to familiarize other NIH organizations with our experiences, to discuss their needs for networking, and to demonstrate existing capabilities. Approximately 60 people attended these talks during FY86.

A multi-user calendaring system was installed on the LAN. Testing and training for use of this system was coordinated by Brian Cole of DMB.

Testing of an Ether3270 server was begun by John Parks of DMB during the fourth quarter of FY86. This server allows PC's attached to the network to emulate

a 3270 terminal for access to an IBM mainframe host such as the NIH Central Utility.

A new generation of software, called 3PLUS, was made available by the company (3COM) that produces our existing software. 3PLUS will allow independent networks to communicate with each other and also allows remote dial-in access to the network. A major advantage of 3PLUS is its ability to use any software designed to run on the IBM PC Network. In order to permit testing of 3PLUS without disrupting daily use of the existing LAN, a separate server was purchased and installed. Testing of 3PLUS and development of a new version of DOware to support 3PLUS was begun during the third quarter of FY86.

During the first half of FY86, DMB and CSL personnel were involved in a coordinated effort to Beta test Ashton-Tate's dBASE III Plus software in a network environment. The test was done on the IBM PC Network. As a result of the test, it was established that multi-user access to data base files can be successfully accomplished with this new product. This software will run on the DCRT LAN when the 3PLUS system is operational.

During the early part of FY87 the 3PLUS software and new version of DOware will be installed on the DCRT LAN. This will allow the DCRT staff in building 31 to communicate with the DCRT staff in building 12A, and will provide dial-in access to the network. A new *DOware User and Administrator Guide* will be written and distributed. It is anticipated that several applications using the multi-user dBASEE III Plus software will be developed to run under 3PLUS. Other multi-user products designed for network use willuse will be tested for suitability to the NIH environment.

If the Ether3270 test shows that 3270 terminal emulation using that approach is adequate, the Ether3270 server will be installed in DMB.

During FY87 we pla to evaluate and report on the IBM Token-Ring network and its relationship to existing LAN efforts.

Seminars regarding our LAN experiences are expected to continue.

Office of Scientific and Technical Communications

William C. Mohler, M.D., Chief

The DCRT Office of Scientific and Technical Communications (OSTC), under the direction of the Deputy Director, DCRT, includes five people in:

- the **DCRT Information Office,** which is responsible for a comprehensive information program directed toward a variety of audiences within and outside NIH. The program is addressed to those whose needs and attitudes have important bearing upon what DCRT strives to accomplish; and
- the **DCRT Library,** which maintains a special collection in computer science, mathematics, and statistics, along with computer applications in biomedical science, engineering, information science, and management. Information resources and services support the activities of DCRT staff and other NIH personnel. Members of the public may use the Library collection on the premises.

Library, Info. Office Handle Wide Information Needs

The Library continued its dual leadership role as an information resource and as an active agent in the development, evaluation and use of computer systems. As an information resource it cooperated with other libraries and information centers by sharing resources. This is accomplished through formal organizations such as Interlibrary Users Association (IUA) of the Washington-Baltimore Area, the Metropolitan Washington Library Council, FEDLINK (the federal library community's consortium), and, at a national level, the Online Computer Library Center (OCLC) network. The number of interlibrary loan requests coming to DCRT continues to far exceed (this year almost 2 to 1) those that DCRT asks from other libraries.

The scope of library services for DCRT and NIH remained at about the same or slightly higher levels compared to FY85, with about a ten percent addition to the registered borrowers list. The staff made room for important new monographs, reports and journals in the existing space by deleting some 500 items and acquiring microfilm copies of journals. Based on continuing experience, they reduced the number of online reference service vendors used.

As an agent in the development and use of computer systems, a large effort went into investigation of data base management systems for use by the Library itself and by others at NIH.

The Librarian answered queries from NIH staff about packages to handle individual or laboratory bibliographic files. To meet the growing interest throughout NIH, she and the Chief of References and Bibliographic Services at the NIH Library organized a demonstration day at the NIH User Resource Center, so that vendors and NIH users could present the merits of several leading commercial packages.

The Library continues to augment its own use of computer systems to improve library operations and access to information. Because of current and prospective use of file server facilities on the DCRT ETHERNET, the Library decided to become a Server Administrator by installing its own 3COM Server facility on the network. The Librarian and Library Technician both are active as instructors and demonstrators of dBASE in DCRT PC training courses and other forums. They continued to acquire, process and circulate selected publications on personal computers for DCRT staff and NIH PC users. The Librarian began serving as a PC Lead User for DCRT staff, primarily in the Office of the Director.

The Information Office began a market research effort to learn more about the makeup and needs of audiences for DCRT communications. A sampling of 300 NIH M.D.'s. and Ph.D.'s. completed the first phase of this project. The resulting analysis has already been used in the communications planning process.

There was heavy involvement in planning of NIH Centennial activities. Slide contributions were prepared for the new NIH slide show. Slides and videotape footage were made available to the producer of the PBS television special featuring NIH. The Information Officer was active in the NIH IO community's joint

efforts for the NIH Centennial, which involve programs to increase public awareness of NIH and to foster careers in the biomedical sciences. DCRT also developed its own contributions to the centennial program for December 1986.

As in previous years the Information Office devoted a large segment of its limited resources to developing and producing publications that together present a comprehensive view of the many activities within DCRT. Nearly 10,000 publications were distributed during the year. This year these included the *1986 Annual Report,* two new editions of *Computing Resources,* several reprints of brochures, and the second annual directory of computer-based image processing facilities and projects throughout NIH. A new item was introduced, a visitors guide, which provides maps and directions to the DCRT complex. Both the *Annual Report* and *Computing Resources* won awards from the Society for Technical Communication. These efforts were accomplished in spite of loss of our typist and the editorial assistant.

The office handled hundreds of requests for information, mostly from NIH staff, but also from diverse groups: hospitals, laboratories, publishers, embassies, and the media. Reporters called from publications--*NATURE, TIME, Newsweek,* and *Government Computing News*--and from radio and television--PBS, Voice of America, NBC, Spanish Information Network, and West German Radio and TV.

Visitors who came to DCRT for briefings and tours included groups from: the Annual Symposium on Computer Applications in Medical Care, *TIME, European Science,* the German Cancer Research Center, a Chinese UNICEF delegation, Mexican National Polytechnic Institute, and the Office of the Deputy Assistant Secretary, DHHS/AMB.

The Office helped arrange an LSM meeting, Conference on Algebra and Lattice Theory, and coordinated DCRT's role in both the MEDINFO86 Meeting and its preliminary workshop for 20 scientists from third world nations. An exhibit was prepared for the annual Minority Biomedical Research Symposium. Publicity was arranged for the May Software Fair held by the NIH User Resource Center, which featured several DCRT presenters.

Because of advances in the industry, the Information Officer reestablished a leadership role in the largely dormant NIH Printing Committee. The Office provided computer typesetting advice and support to NEI, NIGMS, DLA, and to the NIH Editorial Operations Branch. Trials were run using the IBM PC as an input device to typesetting composition systems, both at GPO and at Medical Arts; the Information Officer investigated several desktop publishing systems for potential use at DCRT and/or the NIH Printing Branch; and explored the use of the generic typesetting code announced by the National Information Standards Organization.

Expanded, PC-based Efforts Continue

The Library anticipates continued work for a online catalog to be available on the DCRT ETHERNET. The general collection will include more items about PC's and software packages. Until recently, these were limited to a special collection for the Personal Workstation Office. The Librarian, as a Lead User, will work on expediting staff use of PC's and supported software. All staff will continue to support DCRT activities in PWO and the ETHERNET.

The Information Office is investigating options for more contract help, to maintain the quality and quantity of materials describing the Division's work.

Effort will be made to continue market research efforts; a natural next phase would be an audit of DCRT communications products.

New publications efforts will include a brochure for the new Personal Workstation Office, and an issue of *NIH News and Features.*

We expect to convert the updated DCRT slide show to videotape as well, to allow for easier portability.

Conversion of the computerized file of DCRT scientific papers to a PC-based format will also be a priority. Several packages are now being evaluated.

An NIH desktop publishing system is expected to be operational during the first quarter of FY87. The DCRT Information Office has offered to provide typesetting media and assistance for the pilot tests.

An effort may be made to offer an advanced grammar course for people who have taken technical writing in the past.

Publications

Computing Resources of the Division of Computer Research and Technology. Fall 1985 edition, 28 pp.

Computing Resources of the Division of Computer Research and Technology. Spring 1986 edition, 30 pp.

Division of Computer Research and Technology Fiscal Year 1985 Annual Report, Volume 1. October 1985, 42 pp.

Division of Computer Research and Technology Fiscal Year 1985 Annual Report, Volume 2. October 1985, 76 pp.

Image Processing. Spring 1986, 39 pp.

Visitor's Guide to the Division of Computer Research and Technology. March 1986, 6 pp.

Research Projects

Personal Computer Bibliographic Systems

Ellen M. Chu
with: E. Cerutti (DRS); M. Tipperman (DPM).

This project continues advisory and consultative services to NIH staff seeking automation of personal and laboratory bibliographic files for research and publication. Personal computer packages for storage, retrieval, and reformatting were evaluated for DCRT/PWO. These included: JLOG, PRO-CITE, REFERENCE MANAGER, and SCI-MATE. Three systems were selected for a demonstration day co-sponsored by the DCRT Library, NIH Library, and User Resource Center. All provided for data entry from downloaded online searches, as well as manual data entry; data base module for retrieval and maintenance; and reformatting citations for a variety of publishers' style requirements.

Future plans include continuing assistance and investigation of personal computer bibliographic systems for personal and laboratory files.

Bibliographic Retrieval Systems on Local Area Networks

ELLEN M. CHU.

This project began a year ago, when the DCRT Library joined the initial test stage of the DCRT personal computer implementation on local area networks (LAN). Research into network bibliographic retrieval systems for the library catalog included a survey of general purpose data base management systems (DBMS) and library applications packages. Four DBMS and ten packages have been evaluated to date. In the current absence of network systems, we plan a collaborative development project.

A second network application is development of a system for DCRT LAN users to access and search data on Library journal holdings and current check-in status of recent issues. Plans for the future include develpment of a front-end multi-user interface for the serials system.

Computerized Typesetting Consultation

PATRICIA O. MILLER

DCRT techniques for using WYLBUR to prepare text for direct input to computerized typesetting systems have been made available to others in the NIH public affairs community.

Changes this year in the NIH Computer Center's magnetic media affected the methods used to create typesetting drive tapes; the job control language was revised to handle these changes and new instructions were given to BID's who have used other methods in the past.

Electronic publishing is growing at NIH; this year, NIGMS, NLM, NEI and DLA relied upon our advice. Continuing assistance was provided to the NIH Editorial Operations Branch, which is typesetting the NIH

Scientific Directory/Bibliography via WYLBUR for the first time.

Electronic Typesetting Methods

PATRICIA O. MILLER

This project, begun in FY81, involves collecting and encoding text on magnetic tape for typesetting by GPO. Eliminating rekeying by a typesetter, and thus the galley proof stage of production, has cut typesetting costs 80 percent.

This year, we worked with an NIH consortium to investigate desk-top publishing methods for NIH; attending demonstrations of MBI, IBM PC-RT, ITEK, and Xerox equipment, as well as the TYPE-X trade show.

Medical Arts installed a typesetting system capable of working from floppy disks. Our test of a PC-created floppy failed on this system, which works well with all types of non-PC word processing diskettes. The only successful input was achieved through an optical character recognition scan of hardcopy.

A generic coding scheme was announced this year by the National Information Standards Organization; with the help of GPO, our codes should one day be converted to these methods, to fit a more universal format.

Office of Administrative Management

Kim Regan, Chief

The Office of Administrative Management (OAM) provides administrative support and resources management for DCRT. The Program Planning and Evaluation and Policy and Legislative Analysis functions also reside in the OAM. OAM consists of 16 people (8 temporary or part time), organized functionally into three sections; finance, personnel, and administration.

The **Administrative Management Section** provides primary assistance to the Executive Officer in the overall planning, direction, coordination and execution of the administrative aspects of the Division's program and actively participates in administrative program planning, policy making, and in the resolution of operating problems. Staff in this section provide support for contracts, procurement, travel, training, property, and payroll functions. Resources are monitored and reports are provided to program managers to assist them in accomplishing the Division's missions.

The **Personnel Management Section** supports Division work under many varied and ever changing requirements of the several Federal Personnel Systems used at NIH. The **Financial Management Section** performs the usual budget formulation and execution functions for the Division, and also manages the Project Accounting System (PAS), which provides detailed billing information to users of computer and programming services provided by the Division.

New Management

FY86 was a transition year for OAM, with the retirement of L. Lee Manuel in March. The new Chief, Kim Regan, joined the Division in May, bringing a breadth of administrative and management experience.

The Budget Office continued to carry out annual budget functions for the Division. In addition, a variety of monthly reports were furnished to program managers to inform them of their budgetary status. The office also participated in the annual rate-setting process for Divisional Service and Supply Fund activities, and the ITS Budget Submission.

Staff of the Project Control Office processed requests for new accounts and users of data processing activities, opening 165 new accounts and registering 2,500 new users. The office, with the assistance of staff from other OD/OAM sections, also successfully completed its annual update of information on the over 3,100 accounts and over 17,200 users currently in the Project Accounting System.

The DCRT Personnel Management Section brought closure to the competitive level code project that began in FY85. This was part of an NIH initiative to conduct a position review for assignment of competitive level codes for all occupations in DCRT to determine the retention standing of employees for purposes of reduction-in-force.

The Administrative Management Section processed a variety of procurements to acquire approximately ,000,000 in supplies and equipment for DCRT during FY86. Day-to-day management activities conducted by this staff included: procurement purchases and contracts; processing of travel and training requests; administration of property, space and communications; payroll; and mail/messenger services.

Data Analysis, Automation Plans

The Personnel Management Section is presently gearing up for automating the processing of all personnel actions in conjunction with the DHHS automated system.

Over the next year the new Executive Officer will lead efforts to strengthen the data gathering and analysis that support the decision making process. This will continue to improve the Division's ability to manage and allocate its resources.

DISCRIMINATION PROHIBITED: Under provisions of applicable public laws enacted by Congress since 1964, no person in the United States shall, on the grounds of race, color, national origin, handicap, or age, be excluded from participation in, be denied the benefits of, or be subjected to discrimination under any program or activity (or, on the basis of sex, with respect to any education program or activity) receiving Federal financial assistance. In addition, Executive Order 11141 prohibits discrimination on the basis of age by contractors and subcontractors in the performance of Federal contracts, and Executive Order 11246 states that no federally funded contractor may discriminate against any employee or applicant for employment because of race, color, religion, sex, or national origin. Therefore, the Division of Computer Research and Technology must be operated in compliance with these laws and Executive Orders.

Division of Computer Research and Technology
National Institutes of Health
Bethesda, Maryland 20892